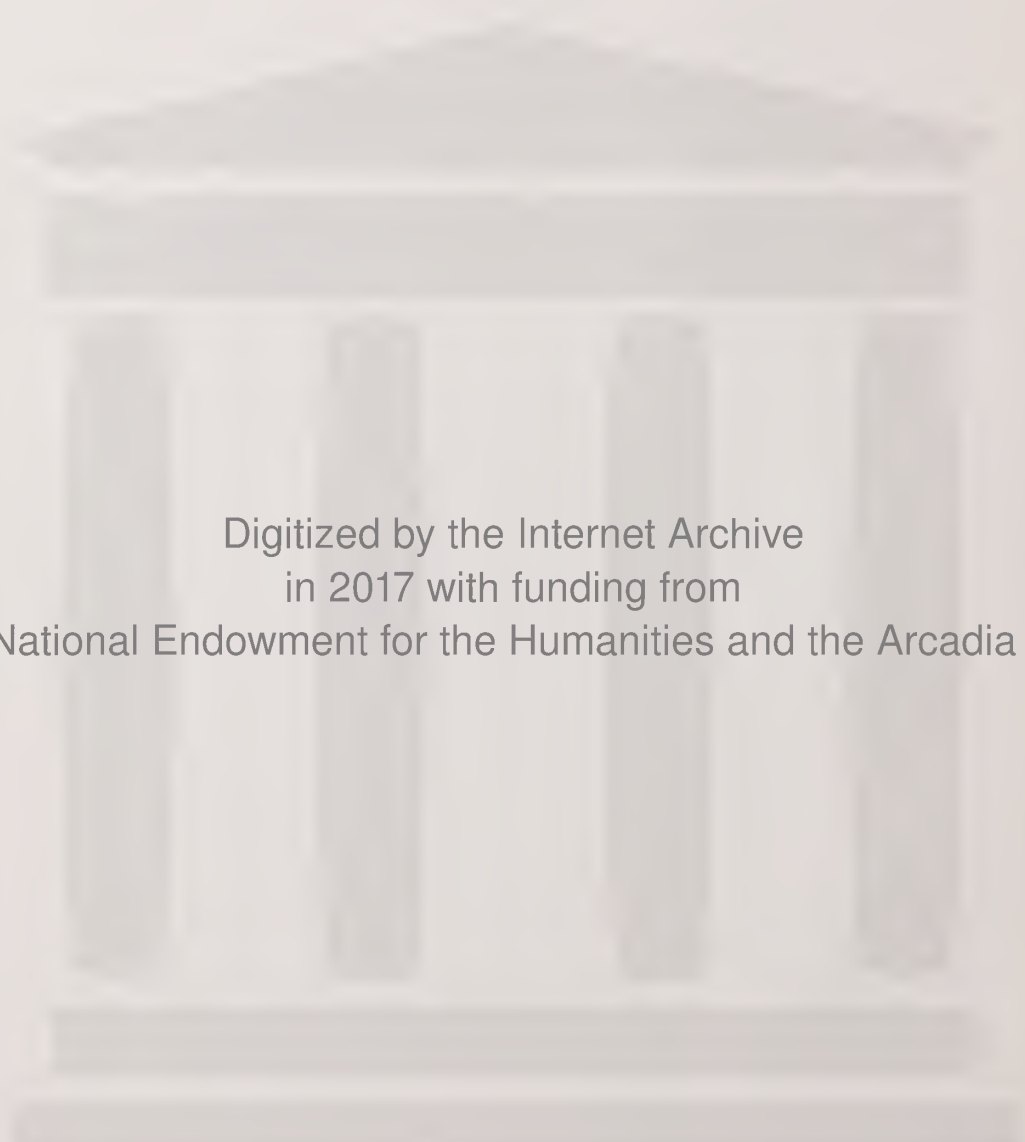




HARVARD MEDICAL LIBRARY  
IN THE  
FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE







Digitized by the Internet Archive  
in 2017 with funding from  
The National Endowment for the Humanities and the Arcadia Fund

# BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

ORGANO OFICIAL



---

VOL. 69

ENERO A DICIEMBRE DE 1977

NUMS. 1-12

---

**Enero:**

Toxicology of Caffeine or Coffee Overdose . . . . .	1
<i>Sidney Kaye, Ph. D.</i>	
Treatment of Thyrotoxicosis with Radioiodine 131 . . . . .	4
<i>Francisco L. Burgos, MD and Julio V. Rivera, MD, FACP</i>	
Intelligence Quotient in Offspring of Oral and Non-Oral Contraceptives Users - Second Part . . . . .	10
<i>Abelardo Fuertes de la Haba, MD, DPH, FACOG, Guillermo Santiago, MD, Ishver S. Bangdiwala, Ph. D, FASA and Carlos A. Roure, MD</i>	
El Consentimiento Informado Médico . . . . .	15
<i>Vicente Font Zelinski, MD, JD</i>	
Epidemiología de Hongos Atmosféricos en Puerto Rico - Parte I . . . . .	25
<i>Carlos López Almodóvar, MD</i>	
Editorial- El Consentimiento Informado Médico - Análisis, Defensa y Opinión . . . . .	29
<i>José L. Cangiano, MD</i>	
Noticias. . . . .	31

**Febrero-**

Determinants of Human Water Contact Patterns in Urban Puerto Rico with Special Reference to Schistosomiasis . . . . .	35
<i>Jan K. Lipes, MD and Robert A. Hiatt, MD</i>	
Recent Advances in the Diagnosis and in the Prevention of Rheumatic Fever. . . . .	45
<i>Angelo Taranta, MD</i>	
Diarrea y Colitis Asociada a Antibióticos . . . . .	55
<i>Carlos H. Ramírez Ronda, MD, FACP y Carlos León Valiente, MD</i>	

Síndrome de Laurence-Moon-Biedl-Bardet. A Propósito de un Caso . . . . .	60
<i>Adolfo Pérez Comas, MD, PhD</i>	
Evaluation of Cellular Mediated Immunity in a Normal Adult Population . . . . .	64
<i>Francisco Robert, MD, José A. Lozada, MD and Francisco J. Muñiz, MD</i>	
Influenza — Treatment and Prevention . . . . .	70
<i>Carlos F. León-Valiente, MD, Carlos H. Ramírez Ronda, MD, FACP and Ramón H. Bermúdez, MD</i>	
Editorial: Water Contact Patterns and Bilharzias . . . . .	74
<i>George V. Hillyer, PhD</i>	
Noticias . . . . .	75
<b>Marzo:</b>	
Heroin Overdose on the Rise Again? (Toxicology of Morphine) . . . . .	77
<i>Sidney Kaye, Ph D and Alma Tudó de Lewis, MSc.</i>	
Management of Long Segment Esophageal Atresia . . . . .	83
<i>Pedro J. Rosselló, MD</i>	
Diarreas Infecciosas Agudas — Diagnóstico y Tratamiento . . . . .	87
<i>Carlos H. Ramírez Ronda, MD, FACP, Carlos León-Valiente, MD y Ramón H. Bermúdez</i>	
Rehabilitación — Filosofía, Alcance y Campo de Acción . . . . .	96
<i>Herman J. Flax, MD, FACP</i>	
Noticias . . . . .	100
<b>Abril:</b>	
Hyperlipoproteinemic Types Among Puerto Ricans: A Final Report . . . . .	102
<i>Marta Cancio, Ph D and José M. León, BS, MT</i>	
Factores Socioepidemiológicos del Uso de Drogas Entre los Estudiantes de las Escuelas Secundarias de Puerto Rico . . . . .	113
<i>Rafaela Robles, Ed.D, Ruth Martínez, B. A., Ana I. Colón, BA y Margarita Moscoso, BA</i>	

The Safety of Percutaneous Arteriography: Indications, Techniques and Results . . . . .	120
<i>R. García Rinaldi, MD, PhD, C. H. McCollum, MD, J. M. Graham, MD, W. W. Defore MD, and M. E. DeBakey, MD</i>	
Coronary Artery Aneurysm: Case Report with Review of Literature . . . . .	129
<i>Rafael A. Cox, MD, Pablo I. Altieri, MD, Fernando Martínez Catinchi, MD and Félix I. León Rivero, MD</i>	
Notas Terapéuticas: Las Penicilinas. . . . .	134
<i>Carlos H. Ramírez Ronda, MD, FACP, Carlos León Valiente, MD y Ramón H. Bermúdez, MD</i>	
Carta al Editor: Síndrome de Hipo-neoglucogenia . . . . .	140
<i>Angel Rodríguez Olleros, MD</i>	
Editorial: La Hiperlipemia en Puerto Rico . . . . .	141
<i>José M. Torres, MD, FACP, FACC</i>	
Noticias. . . . .	143
<b>Mayo:</b>	
Health Maintenance for the Industrial Worker: A Rural Health Experience in Puerto Rico. . . . .	145
<i>José Ramírez Rivera, MD, FACP and Miguel H. Del Toro, MD</i>	
Programa de las Corporaciones para los Trabajadores Incapacitados en Puerto Rico . . . . .	152
<i>Herman J. Flax, MD, FACP</i>	
Successful Repair of a Right Coronary artery — Coronary Sinus Fistula with Associated Left Coronary Arteriosclerosis. . . . .	156
<i>Raúl García Rinaldi, MD., L. Von Koch, MD and Jimmy F. Howell, MD</i>	
Drug Therapy, Cardiac Pacing and Cardiac Surgery in the Wolff-Parkinson-White Syndrome. Report of Two Cases Treated with Cardiac Pacemakers. . . . .	160
<i>Charles D. Johnson, MD</i>	
Coronary Artery Disease: Natural History, Risk Factors and Management. . . . .	167
<i>Henry D. McIntosh, MD, and Kinsman E. Wright, MD</i>	

Noticias. . . . .	176
-------------------	-----

## Junio:

Evaluation of Medical Education: As Developed in The "Curso de Actualización Médica" . . . . .	179
<i>Egidio S. Colón Rivera, MD, José E. Sifontes, MD and Donald W. Keillor, MA</i>	
El Consorcio de Educación Médica del Oeste, Su Historia . . . . .	188
<i>José Ramírez Rivera, MD, FACP</i>	
Cómo se Llega a Ejercer la Medicina en Puerto Rico: 1976 . . . . .	191
<i>José Ramírez Rivera, MD, FACP</i>	
Dígalo en Español or "Say It in English" . . . . .	199
<i>José Ramírez Rivera, MD, FACP and Braulio Quintero, MD</i>	
Pólipos de la Uretra Posterior. . . . .	206
<i>Juan R. Iturregui Pagán, MD y Roberto F. Fortuño, MD</i>	
Editorial: La Escuela de Medicina ante la Educación Médica Continuada . . . . .	211
<i>Carlos E. Girod, MD</i>	
Book Review: Text Book of Black Related Diseases. . . . .	213
<i>Alain Louis-Gustave, Docteur</i>	
Noticias. . . . .	214

## Julio:

Comparative Study of Amikacin(BB-K8) and Gentamicin Activity In Vitro Against <i>Proteus Rettgeri</i> . . . . .	222
<i>Felipe Pérez Rodríguez, MD, Ramón H. Bermúdez, MD, FACP and Carmen Javier de Brau, MT</i>	
Artificial Insemination Donor . . . . .	227
<i>Walter M. Pinedo, MD, FACOG and Rafael Rodríguez Acevedo, MD</i>	
Commentary: Conservative Treatment of Splenic Injuries in Children. . . . .	233
<i>Pedro J. Rosselló, MD</i>	

Las Pruebas Cutáneas y la Alergia a Penicilina . . . . .	237
<i>Carlos F. León Valiente, MD y Carlos H. Ramírez</i>	
<i>Ronda, MD, FACP</i>	

Nuevos Conceptos en la Patofisiología de Hipertensión . . . . .	241
<i>José L. Cangiano, MD</i>	

Noticias . . . . .	246
--------------------	-----

## Agosto:

Fibrosis Quística en Puerto Rico . . . . .	251
<i>José E. Sifontes, MD, Frank Rodríguez, MD, Pedro</i>	
<i>Mayol, MD, Rogelio Menéndez, MD, Efraín Alicea, MD</i>	
<i>y Wilfredo Vélez, MD</i>	

Acute Pre-Infarction Angina . . . . .	258
<i>Pablo I. Altieri, MD</i>	

Dantrolene Sodium: An effective Therapeutic Agent for the Treatment of Spasticity in Children . . . . .	263
<i>José M. García Castro, MD</i>	

Mycotic Pulmonary Artery Aneurysms: A Rare Cause of Fatal Hemoptysis . . . . .	266
<i>Hernán D. Giraldo, MD and José Ramírez Rivera, MD</i>	

Polycystic Liver Disease: Case Report . . . . .	272
<i>A. H. Sarmiento, MD, A. E. Lanaro, MD and D. Vázquez, MD</i>	

Brief Communication — Bleeding Duodenal Ulcer in a Patient Taking Slow-Releasing Potassium Tablets. . . . .	276
<i>Pablo I. Altieri, MD, Carmelo Herrero, MD, Rómulo</i>	
<i>Suero, MD and Armando Ortiz, MD</i>	

Noticias . . . . .	277
--------------------	-----

## Septiembre:

Post Operative Electrocardiographic Changes After Ventricular Aneurysmectomy . . . . .	281
<i>Juan M. Aranda, MD, Stanley Richter, MD, Benjamín</i>	
<i>Befeler, MD and Nabil El-Sherif, MD</i>	



Herencia vs. Ambiente en Diabetes Mellitus. Revisión y Conceptos Propios. . . . .	290
<i>Adolfo Pérez Comas, MD, PhD</i>	
Cardiac Pacemaker Therapy During Pregnancy Labor and Delivery for Heart Block. . . . .	297
<i>Charles D. Johnson, MD</i>	
The Cat-Cry Syndrome, an Unusual Chromosomal Aberration: Report of a Case and Review of the Literature . . . . .	303
<i>Fermín Sánchez Lugo, MD, José M. García-Castro, MD and Luz Carlota Reyes de Torres, MS</i>	
Graphics . . . . .	308
<i>Juan M. Aranda, MD</i>	
Editorial: Diabetes Mellitus: ¿Herencia o Ambiente? . . . . .	311
<i>Francisco Aguiló, Jr.</i>	
Noticias. . . . .	313

**Octubre:**

Hematocrit Level for Puerto Rican Women (Age 20-40) . . . . .	319
<i>Abelardo Fuertes-de la Haba, MD, DPH, FACOG, Héctor Ortiz-Pérez, MD, Ishver S. Bangdiwala, PhD, FASA, and Carlos A. Roure, MD</i>	
Pitfalls in Prescribing Additions for the Elderly . . . . .	327
<i>Migdalia González, MD, Julio E. Pérez, MD, Guillermo Cintrón, MD, Esteban Linares, MD, Edgardo Hernández, MD, Juan M. Aranda, MD</i>	
Abstractos: Trabajos a Presentarse en la Asamblea Anual de la AMPR - Nov.. 7-12, 1977 - Salón de Convenciones del Condado . . . . .	331
Noticias. . . . .	354

**Noviembre:**

Coronary Heart Disease - Sheehan's Syndrome . . . . .	357
<i>Charles D. Johnson, MD</i>	

The Problem Drinker and Traffic Fatalities - Puerto Rico 1976 . . . . .	364
<i>Sidney Kaye, MSc, PhD</i>	
Tétano: Patofisiología, Clínica, Tratamiento y Prevención. . . . .	372
<i>Héctor F. Gorbea, MD y Carlos H. Ramírez Ronda, MD, FACP</i>	
Brief Communication: Temporary Arteritis . . . . .	379
<i>Víctor M. Mojica, MD, Alejandro Franco, MD and Radamés Sierra, MD</i>	
Editorial: Dengue . . . . .	381
<i>Carlos A. Ramírez Ronda, MD, FACP</i>	
Noticias. . . . .	383
 <b>Diciembre:</b>	
Neuroblastoma: Eight Year Experience . . . . .	386
<i>Pedro J. Rosselló, MD, Pedro J. Santiago Borrero, MD and Víctor A. Marcial, MD</i>	
Changing Patterns in Poisoning in Puerto Rico - 1972-1976 . . . . .	391
<i>Sidney Kaye, MSc, PhD</i>	
Editorial: Nefrología 1977 . . . . .	396
<i>Osvaldo Ramírez Muxó, MD</i>	
Discurso Toma de Posesión como Presidente de la Asociación Médica de Puerto Rico . . . . .	398
<i>Rafael Berrios Martínez, MD</i>	
Nota Biográfica: Dr. Rafael Berrios Martínez . . . . .	401
Noticias. . . . .	
Reconocimiento a Arbitros . . . . .	405
Contenido . . . . .	408
Indice de Autores . . . . .	415
Indice de Materias . . . . .	418

# BOLETIN ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

MAR 3 - 1977

THE FRANCIS A. COUNTWAY

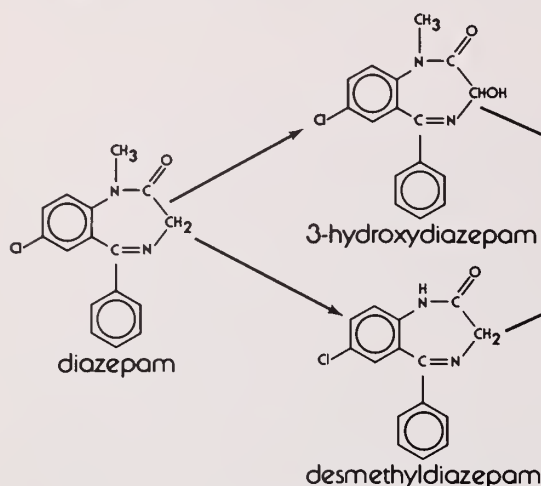
VOL. 69

ENERO 1977

NO. 1



# A pharmacokinetic character all its own



**Valium (diazepam) is a benzodiazepine with a distinctive pharmacokinetic profile**

The pharmacokinetic profile of Valium is one of the characteristics that sets it apart from other benzodiazepines. Consider, in particular, the metabolic pathway of Valium. The three major metabolites of Valium exhibit significant pharmacologic activity—and so, of course, does the parent substance—diazepam itself. All combine to produce the characteristic clinical response seen with Valium. The response you have come to know, to want and to trust.

Pharmacokinetic studies also demonstrate that Valium has a pattern of absorption, distribution, metabolism and elimination that is reliable and consistent. And, although the pharmacokinetics of a drug cannot, at present, be specifically related to its clinical effects, it is clearly a factor that distinguishes one product from another by providing important insights into how each moves through the patient's body.

## Valium® (diazepam) <sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due

to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:**

Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma;

may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients.

Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

## To relieve nausea and vomiting associated with

- postoperative recovery
- radiation therapy
- chemotherapy
- acute situations

(Contraindicated in pregnancy, severe CNS depression, comatose states and in patients who have demonstrated a hypersensitivity to phenothiazines.)

## Three dosage forms with the same 10 mg dosage strength:

**Tablets**—10 mg (thiethylperazine maleate, NF)



**Suppositories**—10 mg (thiethylperazine maleate, NF)



**Injection**—10 mg/2cc ampul (thiethylperazine maleate, NF) for IM use only.



THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

MAR 3 1977

# Torecan®

(thiethylperazine)

Still available in  
Puerto Rico



**Boehringer Ingelheim**

Boehringer Ingelheim Ltd.  
Elmsford, New York 10523

**Torecan®** (thiethylperazine)  
Tablets, Suppositories and Injection

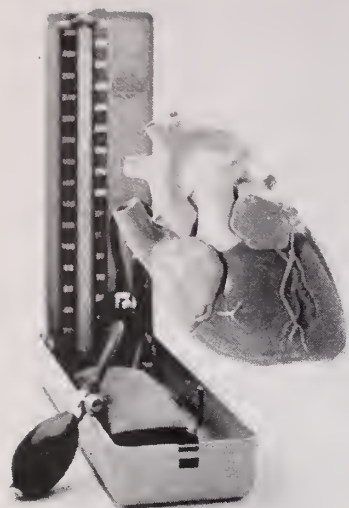
**Contraindications:** Severe CNS depression, comatose states, and in patients who have demonstrated a hypersensitivity to phenothiazines (e.g., blood dyscrasias, jaundice). Because severe hypotension has been reported after the intravenous administration of phenothiazines, this route of administration is contraindicated. The drug is contraindicated in pregnancy.

**Warnings:** Phenothiazines are capable of potentiating CNS depressants as well as atropine and phosphorous insecticides. The drug may impair mental and/or physical ability required in the performance of potentially hazardous tasks such as driving a car or operating machinery. *Postoperative Nausea and Vomiting* When used to control postoperative nausea and vomiting in patients undergoing elective surgical procedures, restlessness and postoperative CNS depression during anesthesia recovery may occur. Possible postoperative complications of a severe degree of any of the known reactions of this class of drug must be considered. Postural hypotension may occur after an initial injection, rarely with the tablet or suppository. Do not use with epinephrine in the treatment of drug-induced hypotension as phenothiazines may induce a reversed epinephrine effect. The most suitable vasoconstrictor agents are levaterenol and phenylephrine. The use of Torecan has not been studied following intracardiac and intracranial surgery. Not recommended for use in children under 12 years of age, or in nursing mothers since safety and efficacy have not been established.

**Precautions:** Convulsions and abnormal movements such as extrapyramidal symptoms have occurred. The varied extrapyramidal symptom complex is more likely to occur in young adults and children. Extrapyramidal effects must be treated by reduction of dosage or cessation of medication. For treatment of nausea and/or vomiting associated with anesthesia and surgery, the drug should be administered by deep intramuscular injection at or shortly before the termination of anesthesia.

**Adverse Reactions:** CNS: convulsions, extrapyramidal symptoms such as dystonia, torticollis, oculogyric crisis, akathisia and gait disturbances, occasional cases of dizziness, headache, fever and restlessness have been reported. Drowsiness may occur initially on injection but is usually alleviated by a reduction in dosage. Dryness of the mouth and nose, blurred vision, tinnitus, sialorrhea and altered gustatory sensation. Peripheral edema of the arms, hands and face. Cholestatic jaundice; cerebral vascular spasm and trigeminal neuralgia have been reported occasionally. The following have occurred with phenothiazine derivatives and should be considered: agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia, pancytopenia, eosinophilia, leukocytosis; miosis, obstipation, anorexia, paralytic ileus; erythema, exfoliative dermatitis and contact dermatitis, jaundice, biliary stasis. Hypotension, rarely leading to cardiac arrest, ECG changes. Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonos, oculogyric crises, tremor, muscular rigidity, akinesia, some of which have persisted for several months or years especially in patients of advanced age with brain damage. Menstrual irregularities, altered libido, gynecomastia, weight gain; false positive pregnancy tests. Urinary retention, incontinence, fever, laryngeal edema and angioneurotic edema, asthma. Hyperpyrexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. ECG changes. While there is no evidence that ECG changes are in any way precursors of any significant disturbance of cardiac rhythm, sudden and unexpected deaths apparently due to cardiac arrest have been reported in a few instances in hospitalized psychotic patients previously showing characteristic ECG changes. A peculiar skin-eye syndrome, which is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea, has also been recognized as a side effect following long-term treatment. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported. *Drug Interactions:* Phenothiazines are capable of potentiating CNS depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorous insecticides. The drug may induce a reversed epinephrine effect on occasion. For complete details, please see full prescribing information.





in hypertension

# ALDOMET®

(METHYLDOPA | MSD)

helps lower  
blood pressure  
effectively...  
usually with no  
direct effect on  
cardiac function—  
cardiac output is  
usually maintained

**Contraindications:** Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity.

**Warnings:** It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

**Use in Pregnancy:** Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

**Precautions:** Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

**Adverse Reactions: Central nervous system:** Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

**Cardiovascular:** Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

**Gastrointestinal:** Nausea, vomiting, distention, constipation, flatus, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

**Hepatic:** Abnormal liver function tests, jaundice, liver disorders.

**Hematologic:** Positive Coombs test, hemolytic anemia. Leukopenia, granulocytopenia, thrombocytopenia.

**Allergic:** Drug-related fever, myocarditis.

**Other:** Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

**Note:** Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

**How Supplied:** Tablets, containing 125 mg methyldopa each, in bottles of 100; Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

**For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486**

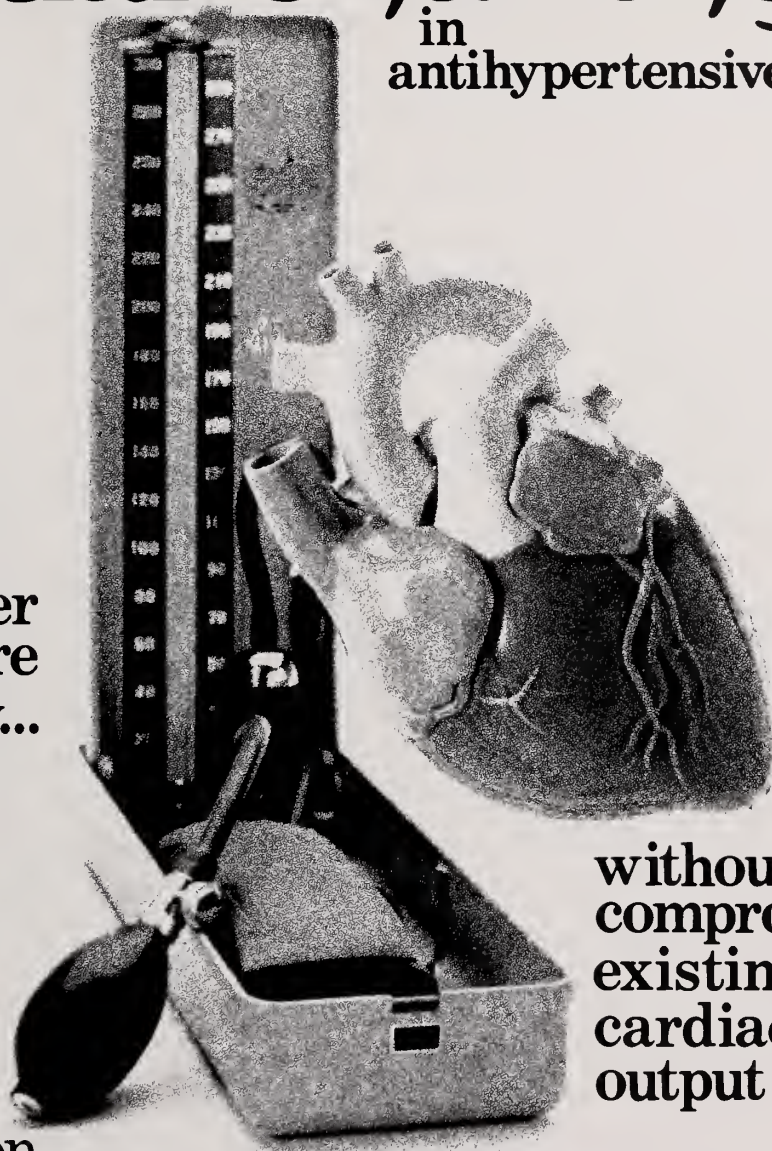
J8AM07 (707)

**MSD** MERCK SHARP & DOHME

# A Dual Challenge

in  
antihypertensive therapy

to lower  
blood pressure  
effectively...



without  
compromising  
existing  
cardiac  
output

in hypertension

TABLETS: 250 mg, 500 mg, and 125 mg

# ALDOMET<sup>®</sup>

(METHYLDOPA | MSD)

helps lower blood pressure effectively...  
usually with no direct effect on  
cardiac function—cardiac output  
is usually maintained

ALDOMET is contraindicated in active hepatic disease, hypersensitivity to the drug, and if previous methyldopa therapy has been associated with liver disorders. It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

For a brief summary of prescribing information, please see following page.

**MSD**  
MERCK  
SHARP  
DOHME



Organo Oficial

Fundado en 1903

Volumen 69

Enero 1977

Número 1

## JUNTA EDITORA

*Jose L. Cangiano, Presidente; Herman J. Flax; Norman I. Maldonado; F. Hernández Morales; Francisco Olazábal, Jr.; Nathan Rifkinson; Enrique O. Vélez García; Antonio J. Grillo; Mario R. García Palmieri; Rafael Villavicencio Jiménez; E. A. Santiago Delpín; Ramón H. Bermúdez; Manuel Martínez Maldonado; José Juan Corcino; Jesús M. Vázquez; Osvado Ramírez Muxó.*

## SECRETARIO DE REDACCION

*Sr. Gregorio Díaz*

### Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

### Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

### Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

## CONTENIDO

Toxicology of Caffeine or Coffee Overdose .....	1
<i>Sidney Kaye, Ph. D.</i>	
Treatment of Thyrotoxicosis with Radioiodine 131 .....	4
<i>Francisco L. Burgos, MD and Julio V. Rivera, MD, FACP</i>	
Intelligence Quotient in Offspring of Oral and Non-Oral Contraceptives Users - Second Part .....	10
<i>Abelardo Fuertes de la Haba, MD, DPH, FACOG, Guillermo Santiago, MD, Ishver S. Bangdiwala, Ph. D, FASA and Carlos A. Roure, MD</i>	
El Consentimiento Informado Médico .....	15
<i>Vicente Font Zelinski, MD, JD</i>	
Epidemiología de Hongos Atmosféricos en Puerto Rico - Parte I .....	25
<i>Carlos López Almodóvar, MD</i>	
Editorial: El Consentimiento Informado Médico - Análisis, Defensa y Opinión .....	29
Noticias .....	31

P O R T A D A : Parque de las Palomas, Viejo San Juan



# TOXICOLOGY OF CAFFEINE OR COFFEE OVERDOSE

Sidney Kaye, Ph.D.

**C**affeine is probably the most widely used of all drugs. It is found in coffee, tea and "cola" drinks. Can it be harmful, or is it a perfectly safe refreshing beverage?

Millions of people drink countless cups of coffee daily — some are bound to drink excessive amounts (more than 5 cups). This could in some cases produce bizarre symptoms.

"Has caffeine overindulgence ever been overlooked and the symptoms diagnosed as psychoneurosis, anxiety type"? This was the question presented by Dr. J. F. Greden, the Director of Psychiatric Research, at Walter Reed Army Medical Center, at the 1974 Spring meeting of the American Psychiatric Society (1). Coffee excesses can elicit symptoms of violent behavior in some persons; but what a feeling of relief to both Physician and patient to see the symptoms completely disappear on the physician's order to stop drinking coffee for 2 days.

The symptoms of caffeine overdose are varied and bizarre and could be easily misinterpreted, as it will be described in the following sections.

**Caffeine Chemical Formula:**  $C_8H_{10}N_4O_2$

## Occurrence (2)

Coffee (coffee arabica): There are about 100 mg of caffeine per cup.

Tea (thea sinensis): Has about 75 mg of caffeine per cup (caffeine + theophylline).

Cocoa (thio broma cocoa): Contains about 200 mg of theobromine per cup.

"Cola" drinks (cola acumenato): Has about 60 mg of caffeine per cup.

## Synonyms

Methyl theobromine; xanthine chemical group; trimethyl xanthine.

Theophylline and theobromine are related xanthines that are pharmacologically similar to caffeine.

## Uses

Caffeine is a powerful CNS stimulant, a mild diuretic and has been used as a mild antidepressant. It maintains wakefulness (Antihypnotic), decreases drowsiness, and fatigue, while increasing clearness of the mental process acting as a cortical stimulant. It is incorporated in "cold treatment or pain tablets" such as APC and others.

Caffeine is most commonly used in the form of coffee (by far) as a "pick up" mental stimulant, since it decreases feeling of sleepiness, especially at breakfast and also the feeling of boredom or tiredness at midmorning and midafternoon. Many millions of cups of coffee are consumed daily at the customary "coffee breaks".

## Physical Properties

Caffeine is a white crystalline and shiny powder with a melting point of  $236^{\circ}C$  and is a weak base.

## MLD

Very few deaths have been reported by its use and probably when used in excess of 10 grams. The blood lethal level are probably in excess of 15 mg percent.

## Remarks

No deaths have been reported by an overdose

of drinking coffee, — but an overdose of coffee of more than 5 cups per day may have a direct dose related effect on the central nervous system, and may affect the heart and its rhythm, blood vessel diameter, coronary circulation and increase blood pressure, urine volumen and gastric secretions. These effects are capable of producing bizarre signs and symptoms which are very baffling, i.e.: High fever or low grade fever unresponsive to persistent antibiotic treatment (3), psychoneurosis (anxiety) unresponsive to Diazepam (1) and paroxysmal atrial tachycardia (4).

### Symptoms (1-9)

The symptoms vary with acquired or inborn tolerance, but in general the patients may complain of light headedness, dizziness, breathlessness, chest discomfort, nervousness, irritability, tremulousness, muscle twitching, tension headache, insomnia (difficulty in getting to sleep or staying asleep), psychoneurosis (anxiety), lack of appetite, loss of weight, restlessness, silliness, elation, euphoria, confusion, disorientation, excitation, and even violent behavior with wild, manic screaming, kicking and biting, progressing to semi stupor (1).

Heart palpitations, extra systoles, tachycardia and arrhythmias, may be present.

Increased gastric secretions and gut motility, nausea, vomiting, diarrhea, epigastric pain, may be produced and elevated plasma levels of fatty acids, and diuresis may be found.

The symptoms intensify with increased dose, which now may produce: high fever, dehydration, convulsions, severe cerebral edema, hypotension, circulatory failure, respiratory failure, and death.

### Treatment

Coffee over *indulgence* is overlooked many times because the bizarre symptoms may resemble and masquerade as an organic or mental disease (1).

If the above symptoms subside after discontinuation of the intake of coffee within 36 hours, it then could be safely assumed they were due to caffeinism.

The symptoms may reappear if patient again drinks coffee excessively (1).

### Comments

Heavy coffee drinkers report tolerance, including cross tolerance with other xanthine containing beverages. Physical dependence with mild withdrawal symptoms such as: headache, "craving", irritability, nervousness, restlessness, lethargy, and inability to work effectively may occur on abstinence.

Coffee can have a more profound effect on the old and on the very young. Limited amounts may be allowed to the old — but surely we should question the practice of feeding coffee to the infant (or child) as in the practice in Puerto Rico.

If we would limit our coffee intake, we then could surely find merit in drinking it in moderation, — since there are few moments as pleasant as when awakening with the aroma of coffee in the air: Coffee as a way to start the day, and coffee to wind up a good meal would be difficult to replace. This apparently is also the view of Dr. Varsrub, the Senior Editor of the JAMA who goes much further when he wrote: "At a time when our life's pleasurable habits are undergoing a process of attrition, when many culinary delights are prescribed, it is comforting to know that a cup of coffee — sine sugar and cream, of course — need not be a medical "no - no" (9).

### Summary

Coffee can be a very enjoyable part of our diet when taken in moderation. But coffee when taken in excess of more than 5 cups can produce bizarre symptoms that can easily be misleading and terrifying. These symptoms vary widely between individuals and can show up as cardiac, circulatory, gastric or mental deviations from normal. Symptoms that may resemble psychoneurosis (anxiety) can also be attributed to coffee overdose.

If only the attending physician were given the hint and prescribed "stay off coffee for 2 days", the symptoms would dramatically disappear.

Some persons are more susceptible than others; and the very old and very young are most vulnerable.

### References

1. Creden, J. F.: Anxiety or Caffeinism: a Diagnostic

- Dilemma, to appear in Amer. Jour. Psych.
2. (a) Goodman, L. S., & Gilman, A., The Pharmacological Basis of Therapeutics, The Macmillan Co., N. Y., 3rd. Ed., 1965.  
(b) Ibid - 4th. Ed., 1970.
  3. Reimann, H. A., Caffeinism: a cause of long - continued, low grade fever, JAMA 202: 1105, 1967.
  4. Personal experience.
  5. Silver, W., Insomnia, tachycardia, and cola drinks, Pediat. 47: 635, 1971.
  6. Flynn, J. T.: Arrhythmias related to coffee and tea, JAMA, 211: 663, 1970.
  7. Harrie, J. R.: Caffeine and headache, JAMA, 213: 628, 1970.
  8. Goldstein, A., Warren, R.: Psychotropic effects of caffeine in man. I. Individual differences in sensitivity to caffeine induced wakefulness. J. Pharmacol. & Exp. Ther., 149: 156, 1965.
  9. Varsrub, Samuel, Senior Editor, JAMA, An Editorial: "A break for the coffee break:", JAMA, 231: 965, 1975.
  - 10.(a). Routh, J. I., Shane, N. A., Arredondo, E. G., Paul W. D., Det. of caffeine, Clin. Chem., 15: 661, 1969.
  - 11.(b). Routh, J. I., Methodology for analytical toxicology, I. Sunshine (Ed), C. R. C. Press, Cleveland, 1975.
  - 11.Garriott, J. C., Jones, Susan, Caffeine conc in blood after taking coffee, coca cola or caffeine, Foren. Sci. Gazette, 5: 2, 1974.
  - 12.Fioresi, F.: Clin. Path., Mario Stefanini (Ed), Grune and Stratton, Vol. II, N. Y., 1969.
  - 13.Sunshine, I., (Ed) Methodology for Anal. Tox., C. R. C. Press, Cleveland, 1975.
  - 14.Davidow, B., Petri, N. L., Quame, B., Tech. Bull., Reg. Med. Tech., 38: 298, 1968.



# TREATMENT OF THYROTOXICOSIS WITH RADIOIODINE 131

Francisco L. Burgos, MD  
Julio V. Rivera, MD, FACP

Hertz (1) and Hamilton (2) first used radioiodine in the treatment of Graves' disease in 1941. In the early exploratory years radioiodine was used cautiously because of fear that radiation might cause thyroid cancer, leukemia or genetic damage. The initial concern about these possibilities has not been supported by experience to this date and arbitrary barriers to the use of radioiodine have gradually fallen (3). At present it is one of the most frequently used modalities of treatment for thyrotoxicosis.

The advantages of radioiodine therapy include absence of mortality, vocal cord paralysis, hypoparathyroidism, discomfort or scar, and the fact that it is the least expensive form of treatment.

Even though radioiodine has been in use in the treatment of thyrotoxicosis for over 30 years, the dosage schedules and their ultimate effect are not yet well established (4, 5). Recently, reduction in originally prevalent dosages has been proposed as a way of avoiding an increasing incidence of post-therapy hypothyroidism (6).

After a brief experience with then generally accepted doses of radioiodine which uniformly led to early hypothyroidism, we tentatively established in 1958 our guidelines for treatment as follows: a) patients younger than 30 years were given a trial of treatment with methimazole for at least one year; if permanent remission did not occur, radioiodine was then given; b) older patients received radioiodine as the initial treatment; c) dose of radioiodine varied from 2.5 to 6 mCi depending on the severity of the disease, the size of the gland and the presence of palpable nodularity; d) additional doses of  $^{131}\text{I}$  were given

as necessary, but not sooner than six months after the previous one; e) we aimed at rehabilitation of patients rather than at complete clinical or "laboratory" remission of the disease. These policies have been maintained till the present time. It should be noted that dosages used fall within the "small dose" range recently in use in several clinics.

The aim of this study was the evaluation of the effectiveness of this treatment program.

## Material and Methods

The records of all patients treated with radioiodine for thyrotoxicosis at the San Juan Veterans Administration Hospital between 1959 and 1972 were reviewed and pertinent data about their condition at the time of first treatment was extracted. An attempt was made to re-examine each one of them to ascertain his present condition. This examination included review of clinical status, thyroid scintigram, radioiodine uptake, serum thyroxine and  $\text{T}_3$  resin uptake.

Statistical study of various features as reported below utilized Pearson's Correlation Coefficient.

## Results

### Patient Sample

A total of 57 patients were treated with radioiodine. Four of them had thyroidectomy after radioiodine treatment; one of them had an autonomous nodule, and the other three a multi-nodular goiter. Adequate follow up examination was not possible in 13. These 17 patients were excluded from the tabulations.

All patients were male, their ages ranging from 19 to 68 years (Table I). The duration of the illness before radioiodine therapy varied from less than 3 months to 48 months. Sixty five percent of the patients

---

*From the Medical and Nuclear Medicine Services, San Juan Veterans Administration Hospital and the Departments of Medicine and Radiological Sciences, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.*

TABLE I  
AGE DISTRIBUTION

Age (years)	No.	Percent
19 - 30	8	20
31 - 40	14	35
41 - 50	14	35
51 - 60	2	5
61 - 70	2	5

TABLE II  
DOSE OF RADIOIODINE

Dose (mCi)	Initial Dose No.	Total Dose No
2.1 - 4.0	28	18
4.1 - 6.0	11	10
6.1 - 8.0	1	4
8.1 - 10.0		6
10.1 - 12.0		0
>12.0		2

had received antithyroid drugs which explains the long duration of disease prior to radioiodine therapy.

On the basis of clinical and laboratory findings, the disease was judged as severe in 9 patients, moderately severe in 28 and mild in 3. The clinical finding that best correlated with severity of the disease was weight loss. The three patients classified as mild had less than 15 percent weight loss with a mean of 9.8 percent. Those classified as moderate were scattered but had a mean of 17.7 percent weight loss and those classified as severe had a mean weight loss of 27.5 percent (Figure 1).

#### Radioiodine Therapy

The initial therapeutic dose of radioiodine ranged from 2.5 to 8.4 mCi, with an average of 3.8 mCi. The majority (70 percent) of patients received up to 4 mCi as a first dose (Table II). The time from initial treatment with radioactive iodine to follow up examination ranged from 2 to 14 years with a mean of 5.8 years.

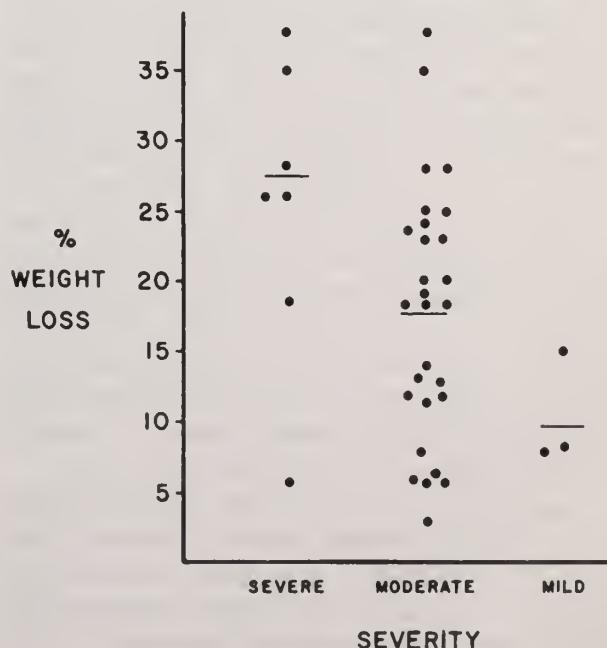


Figure 1

TABLE III  
RESULTS OF RADIOIODINE THERAPY

Thyroid Status	Interval Since Initial Dose		Final (2-14 yrs.)
	up to 12 months	up to 18 months	
Euthyroid	20	25	28 (70 percent)
Hypothyroid	4	4	9 (22.5 percent)
Hyperthyroid	16	11	3 (7.5 percent)

TABLE IV  
RADIOIODINE DOSE AND FINAL RESULTS

Result	Patients	Doses	<sup>131</sup> I Dose 1 (mCi)	
			Initial	Total
Euthyroid	20	1	3.71	
Euthyroid	8	2 - 3	3.00	7.17
Hypothyroid	7	1	4.67	
Hypothyroid	2	2 - 3	4.85	11.30
Hyperthyroid	3	1 - 4	3.33	10.25

The eventual results of treatment are summarized in Tables III and IV.

Twenty nine patients received only one dose of radioiodine. This resulted in an euthyroid state of 20 of them. This was attained within six months in 14 patients and by the end of one year in three more. In three others achievement of a normal state required up to 30 months.

Seven other patients required two doses and one needed three doses to attain an euthyroid state. Among these patients this result was delayed beyond one year in six.

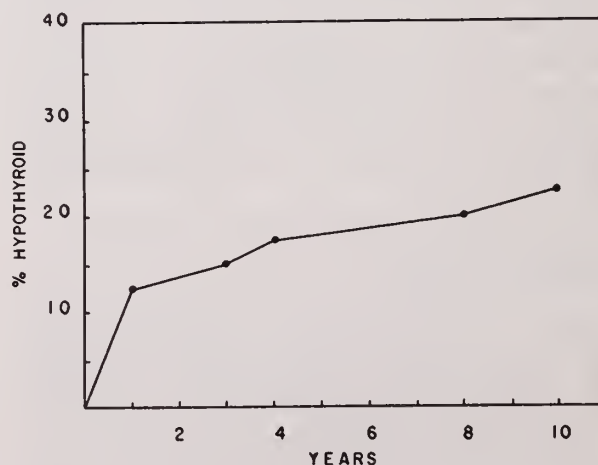
Thus in patients whose only treatment was radioiodine, a persistent euthyroid state was achieved within one year in 20 patients, within 18 months in 25 and by the end of 30 months in 28 (70 percent).

Hypothyroidism occurred in 9 (22.5 percent) subjects whose only treatment was radioiodine. In five of them onset was within one year of therapy, usually after a single dose. In the four other patients hypothyroidism followed two to ten years after radioiodine. All but one of the latter had received only one dose (Figure 2).

In two other patients sub-total thyroidectomy for multi-nodular goiter following radioiodine therapy re-

sulted in hypothyroidism. One of them was operated because of poor response to multiple doses of radioiodine (total 31 mCi). The other one had a hypoactive nodule which was suspected to be malignant. Histological diagnosis was hyperplasia with involutional changes.

In three patients thyrotoxicosis was still present at the



time of last examination. One of them had received a total of 9.2 mCi of radioiodine divided in three doses over a period of two years. Another had been given four doses totalling 17 mCi. The third patient had refused further treatment after a single, 4.5 mCi, dose. These patients received methimazole, propranolol or both during most of the intervals.

The average dose received by those patients who are euthyroid after a single dose of radioiodine was 3.71 mCi (Table IV). The patients who became hypothyroid after a single dose received an average dose of 4.67 mCi, while those who became euthyroid after two to three doses received an average 7.17 mCi. The initial dose in the last group averaged 3.00 mCi. The difference in initial dosage level between the euthyroid and hypothyroid groups is statistically significant ( $\chi^2 = 0.7$ ) but not that between the euthyroid and hyperthyroid groups.

No significant difference was found as to the severity of the disease, the gland size or laboratory results at the time of initial examination in the various groups and the eventual results of treatment ( $\chi^2 = 0.1$ ). Figures 3 and

4.

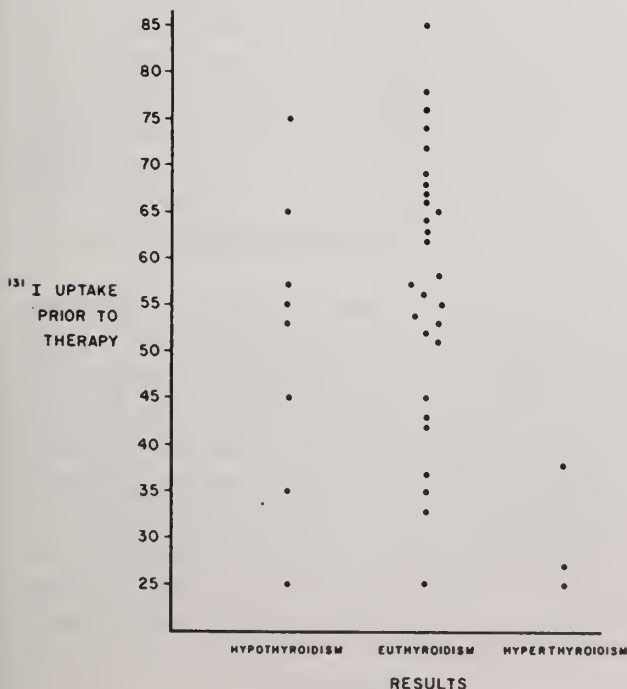


Figure 3

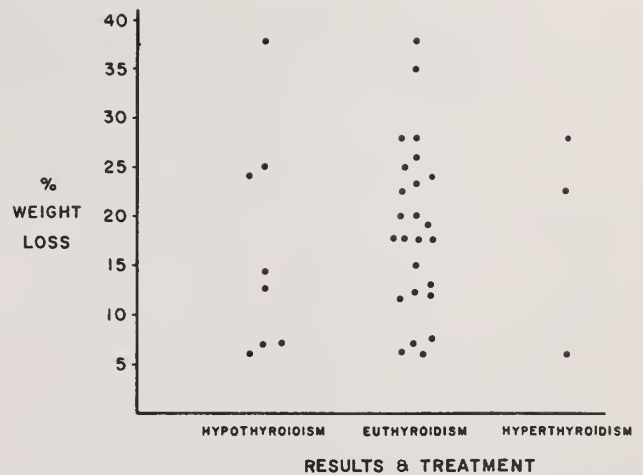


Figure 4

## Discussion

The success of any therapeutic program, even when it involves measures of well established merit, may be affected by various factors which may weight the results in a positive or negative direction. Socio-economic, psychological, cultural, genetic and, as in the case of institution-centered programs, even administrative elements may influence the final results. For this reason evaluation of therapeutic programs in different patient populations is always advisable and interesting. Martínez de Andino and Rodríguez (7) first reviewed an experience with radioiodine in Puerto Rico. The present one is the first study to be published.

The results of this small study illustrate the advantages and some of the problems that characterize treatment of thyrotoxicosis with radioiodine.

The highly satisfactory results obtained in most of the patients must first be emphasized. Complete rehabilitation was achieved within 18 months in 25 patients and eventually in a total of 28 (70 percent).

Although all the patients were hospitalized briefly for treatment, this was usually due to administrative rather than medical reasons. Identical treatment could have been given on an out-patient basis thus minimizing costs further. Morbidity and mortality were totally absent. This contrasts with surgical treatment where, in the best hands, significant morbidity and rare mortality must be accepted and hospitalization can not be avoided.



TABLE V  
HYPOTHYROIDISM AFTER RADIOIODINE

	No. of Patients	Dose (ave.) mCi	Percent Hypothyroid Years After Treatment			
			1	2	5	10
Douglas (11)	94	8.7	37.8	45.6	54.4	70.0
Nofal (17)	797	10.0	40.8	44.5	51.9	69.5
Dunn (12)	234	6.8	20.0	25.0	27.0	37.0
Rapoport (10)	85	3.6	7.1	11.7	16.4	----
Smith & Wilson (18)	276	5.0	7.9	13.1	29.0	----
Smith & Wilson (18)	270	2.8	4.3	6.2	7.4	----
Burgos	40	3.8	12.5	12.5	17.5	22.5

In a small, but significant, number of cases disability due to thyrotoxicosis was more prolonged. The factors responsible for this were poor response to the initial dose of radioiodine and failure of one of the patients to accept further treatment.

Three of the patients whose response to initial radioiodine therapy was poor had nodular glands. This agrees with the experience of others (8) who have shown that considerably larger doses of radioiodine are frequently required for the control of multi-nodular goiters than for diffuse goiters. Because it was our hope to avoid hypothyroidism as much as possible, our initial dosage was perhaps unduly restricted. Surgical intervention led to hypothyroidism in two patients probably as a result of the effect of radioiodine on the thyroid remnant.

Prolongation of disability is the most important problem related to therapy with anti-thyroid drugs. After constant medication continued usually for at least two years persistent remission is achieved in 45 to 72 percent of patients (9). In the remaining patients the problem of definitive therapy has only been deferred. The question of patient compliance with medication can be a major one in certain population groups and the economic factor can not be disregarded.

Early-onset hypothyroidism due to radioiodine is dose-related and its incidence can be reduced by limiting the initial medication (4). A reliable method for estimating the correct dose has, however, not been devised (5, (10). Thus, as in our group, it is difficult to avoid a small incidence of hypothyroidism occurring during the first year or two post therapy.

Delayed-onset hypothyroidism has been the main

problem associated with radioiodine therapy (4), (6), (10), (11), (13), (Table V). Although some evidence is accumulating that this problem can at least be delayed by reduction in radioiodine dosage (6), (10), long range studies will be required before this is established. Another approach to the problem has been the use of another radioactive iodine isotope ( $^{125}\text{I}$ ) which because of its lack of beta radiation is less liable to result in damage to the genetic apparatus of the cell thus allowing cell replacement (4), (14). This method of treatment also requires further evaluation. The fact that hypothyroidism may follow surgical treatment (15) suggests that this phenomenon may be a manifestation of the autoimmune mechanisms of the disease which may be accelerated by treatment of various types. In our cases delayed onset hypothyroidism occurred in a relatively small number of cases (22.5 percent) but it is uncertain to what extent this apparently reduced rate is due to the relatively small radiation doses administered or to the short period of follow up.

The need for continued surveillance of all patients with Graves' disease regardless of the modalities of treatment employed must be emphasized. Serial determinations of thyroid hormones, thyrotropin and lipids should provide early warning of the onset of thyroid failure and insure prompt institution of substitution therapy (16).

We hope that the publication of our results will stimulate others in Puerto Rico to review their experiences in the management of this intriguing disease.

### Summary

Forty men treated with radioiodine ( $^{131}\text{I}$ ) in doses



ranging from 2.9 to 17 mCi (average, 3.86 mCi) were re-examined 2 to 14 years after initial treatment. An euthyroid state was attained in 20 patients in one year and in 28 (70 percent) in up to 30 months. Five developed hypothyroidism by the end of one year and four more (total 9 or 22.5 percent) did so 2 to 10 years thereafter. Sixteen were still toxic at the end of one year and three (7.5 percent) remained so after 2 to 5 years. No complication of therapy other than hypothyroidism was observed.

### Resumen

Se examinaron cuarenta varones tratados por tirotoxicosis con radioyodo ( $^{131}\text{I}$ ) en dosis de 2.9 a 17 mCi (media, 3.86 mCi), de 2 a 14 años antes. Veinte de ellos habían llegado a un estado eutiroides al final de un año y 28 (70 por ciento) antes de 30 meses del comienzo de la terapia. Cinco se tornaron hipotiroideos antes de un año y 4 mas (total 9, 22.5 por ciento) entre 2 y 10 años después. Diez y seis enfermos continuaban hipertiroideos al cabo de un año y tres (7.5 por ciento) 2 a 5 años respectivamente después de tratamiento. No se observaron otras complicaciones de tratamiento

### Acknowledgment

We thank Dr. Arthur Trevino for his assistance in the statistical study of the data and Ms. Pilar López Nito for the clerical work.

### References

1. Hertz, S. and Roberts, A.: Application of radioactive iodine in therapy of Graves' disease - J. Clin. Invest. 21: 624, 1942.
2. Hamilton, J. G. and Lawrence, J. D.: Recent application of radio-phosphorus and radioiodine - J. Clin. Invest. 21: 624, 1942.
3. Starr, P. Jaffe, H. L. and Oettinger, L., Jr.: Later results of  $^{131}\text{I}$  treatment of hyperthyroidism in 73 children and adolescents: 1967 follow up - J. Nucl. Med. 10: 586, 1969.
4. Dworkin, H. J.: Treatment of diffuse toxic goiter with  $^{131}\text{I}$  - Seminars of Nucl. Med. 1: 399, 1971.
5. Bland, W. H. and Hays, M. T.: Graves' disease in the male. A review of 241 cases treated with an individually calculated dose of sodium iodine I  $^{131}$  - Arch. Intern. Med. 129: 33, 1972.
6. Hagen, F. A., Ovellette, R. P. and Chapman, E. M.: Comparison of high and low dosage levels of  $^{131}\text{I}$  in the treatment of thyrotoxicosis - N. Engl. J. Med. 277: 559, 1967.
7. Martínez de Andino, A. and Rodríguez, A. L.: Clinical experience with radioactive iodine in the treatment of hyperthyroidism - Presented at the Regional Meeting of the American College of Physicians, San Juan, Puerto Rico, October 7, 1960.
8. Eller, M., Silver, S., Yohalem, S. B. and Segal, R. L.: The treatment of toxic nodular goiter with radioactive iodine: 10 years experience with 436 cases - Annals of Intern. Med. 52: 976, 1960.
9. Hershman, J. M., Givens, J. R., Cassidy, C. E. and Astwood, E. B.: Long term outcome of hyperthyroidism treated with antithyroid drugs - J. Clin. Endocrinol. Metab. 26: 803, 1966.
10. Rapoport, B., Caplan, R. and De Groot, L. J.: Low dose sodium iodine  $^{131}\text{I}$  therapy in Graves' disease - J. Am. Med. Assoc. 224: 1610, 1973.
11. Douglas, J. G.: The Vanderbilt experience with  $^{131}\text{I}$  in treatment for Graves' disease - Southern Med. J. 66: 92, 1973.
12. Dunn, J. T. and Chapman, E. M.: Rising incidence of hypothyroidism after radioactive iodine therapy in thyrotoxicosis - N. Engl. J. Med. 271: 1037, 1964.
13. Beling, U. and Einhorn, J.: Incidence of hypothyroidism and recurrence following  $^{131}\text{I}$  treatment of hyperthyroidism - Acta Radiol. 56: 275, 1974.
14. Siemsen, J. K., Wallack, M. S., Martin, R. B. and Nicoloff, J. T.: Early results of  $^{125}\text{I}$  therapy of thyrotoxic Graves' disease - J. Nucl. Med. 15: 257, 1974.
15. Bronsky, D., Diamko, R. T. and Waldstein, S. S.: Post-therapeutic myxedema. Relative occurrence after treatment of hyperthyroidism by radioactive iodine ( $^{131}\text{I}$ ) or sub-total thyroidectomy - Arch. Intern. Med. 121: 113, 1968.
16. Toft, A. D., Seth, J., Hunter, W. B. and Irvine, W. J.: Plasma thyrotropin and serum thyroxine in patients becoming hypothyroid in early months after iodine -  $^{131}\text{I}$  - Lancet 1: 704, 1974.
17. Nofal, M. McCall: Treatment of hyperthyroidism with sodium iodide  $^{131}\text{I}$  - JAMA 197: 605, 1966.
18. Smith, R. N. and Wilson, G. M.: Clinical trials of different doses of  $^{131}\text{I}$  in treatment of thyrotoxicosis. Brit. Med. J. 1: 129, 1967.

# INTELLIGENCE QUOTIENT IN OFFSPRING OF ORAL AND NON-ORAL CONTRACEPTIVE SECOND PART

Abelardo Fuertes de la Haba, MD, DPH, FACOG

Guillermo Santiago, MD

Ishver S. Bangdiwala, Ph.D., FASA

Carlos A. Roure, MD

This is the second part of a series of continuing investigations on the possible influence on the intelligence (commonly measured by Intelligence Quotient, I. Q.) of offspring whose mothers used oral contraceptives prenatally. The results of the first part were published in 1974 (13).

Since oral contraceptive steroids are being employed by over 50 million women all over the world as a method of family planning, it is essential to look for all possible effects on the offspring of mothers who used this medication. In a series of studies through a controlled experiment, we have analyzed several parameters concerning the use of contraceptives and their effects on several characteristics of users as well as the intelligence of their offspring (9, 10, 11, 12, 13). We have also studied the dosage of medication taken prenatally as well as age of children's mothers in relation to the I. Q. Studies made by others reflect results directly or indirectly to some extent in the related field (1, 3, 4).

Socio-economic factors are important variables that may affect the child's later development and its intelligence (5, 6, 7). These factors are also important in judging perinatal influence which may affect the child's intelligence; hence in this paper we have studied the children in the upper, medium and lower socio-economic levels, measured according to the scale prepared by the Council on Higher Education of Puerto Rico (8).

## Background of Study

The Maternal Health Study Program was designed in 1961 as a result of Dr. Gregory Pincus' interest in the incidence of genital and breast cancer in women who were taking progestational agents. It was initiated in Río Piedras, Puerto Rico, and later extended to the municipalities of Caguas and Ponce. This program has been the matrix for long-term studies designed to reach a clear understanding on the uses and effects of oral contraceptives.

Women admitted to the Maternal Health Study Program met basic minimum qualifications such as: age 21 to 39 years; at least one normal pregnancy; no prior use of oral contraceptives or intrauterine devices. Each candidate, before admission to the program, agreed to use the contraceptive that would be prescribed to her.

Once a woman was found eligible and prior to the physical examination, she was assigned at random to an experimental (oral) or control (non-oral) group \* which she was to follow throughout the experiment.

The subjects of the present study were the 5,465 women admitted at the Río Piedras clinic between 1961 and 1969. The randomization procedure mentioned earlier assigned 2,741 women (50.2 percent) to the study group (oral) and 2,724 (49.8 percent) to the control group (non-oral contraceptives). A comparison of the main characteristics of both groups was made, showing that the randomization procedure was successful and, thus, the groups were considered identical and, therefore, comparable (9).

---

*From the Department of Obstetrics and Gynecology, Department of Psychiatry, University of Puerto Rico School of Medicine and Department of Graduate Studies, University of Puerto Rico.*

\* - The oral group used norethynodrel 5 mg. mestranol .075 mg. (Enovid). Total Steroid: 5.75 mg./tab. G. D. Searle and Co., Chicago, Illinois. The control group used such methods as diaphragm, prophylactics, suppositories, etc.

TABLE I  
CORRELATION BETWEEN AGE AND INTELLIGENCE QUOTIENT (I.Q.)  
FOR ORAL AND NON-ORAL GROUPS

Group	Number in Group	Age in Months (AIM)		I. Q. Score		Correlation Coefficients (r)
		mean	s. d.	mean	s. d.	
Oral	96	73.3	8.7	85.08	13.7	0.121 (NS)
Non-oral	114	73.9	8.1	85.54	11.4	0.026 (NS)

(NS) Coefficient of correlation (r) is not significant at 5 percent level.

### Characteristics of Offspring

The next step was to identify the mothers who had had offspring after admission. During the period (1961-69), 398 children were born to these 5,465 women; 229 (57.5 percent) of them were between ages 5 and 8 at the time of the study, an age range suitable for the psychological tests to be used. Of these 229 children, 210 (91.7 percent) were included in the study. The other nineteen cases (11 in oral and 8 in non-oral) were excluded either because the children were dead or because they had moved out to other communities, making it difficult to bring them in for the required tests.

The 210 subjects of the present study were distributed as follows: 96 children belonged to the group whose mothers used oral contraceptives and 114 to that of the women who used non-oral contraceptives.

The study group (oral) had 41 boys (42.7 percent) and 55 girls (57.3 percent) while the control group had 60 boys (52.6 percent) and 54 girls (47.4 percent). Thus the group of 210 children was made up of 101 males (48.1 percent) and 109 females (51.9 percent). The experimental group had a higher percentage of girls than the control group (+ 9.9); the control group consequently had a higher percentage of boys (+ 9.9). There was no statistical differences between the distributions by sex of the two groups.

The ages of the children in the study for I. Q. test fluctuated between 5 and 8 years, as indicated earlier.

The percentage distribution within the age categories indicated that more girls in the study group than in the control (non-oral) group fell into the lower age categories. Within the subgroups a higher percentage of boys than girls figured in the 5 and 7-8 year old categories, while more girls than boys were six years old. There was no significant difference between the average ages of the two groups of children: 6.1 years for the study group (oral) and 6.2 years for the control group (non-oral).

### I. Q. Scale

There are two scales commonly utilized in the United States of America to measure the intelligence of the child: one of them is the Stanford-Binet (S. B.) and the other one is Wechsler's (W). In our experiment, it was decided to use the Wechsler's (W) as that is the scale which has been normalized and adapted for Puerto Rico; the Stanford-Binet (S. B.) scale is not.

The average Puerto Rican child's I. Q. score is about 12 points lower than the average American child's, according to the equivalent norms prepared by the Puerto Rican Department of Education (14). An I. Q. score of eighty eight (88) of a Puerto Rican child is equivalent to a score of one hundred (100) on the scale of I. Q. norms of United States children. The children in Puerto Rico with I. Q.'s. between 77 and



**TABLE II**  
**AVERAGE DOSAGE CONSUMED BY MOTHERS AND AVERAGE I.Q. OF**  
**CHILDREN BY SOCIO-ECONOMIC GROUP**

Socio-Economic Group	Number of Patients	Average Dosage Consumed	Average I. Q. of Children
Upper	12	25.8	91.83
Middle	66	32.1	85.73
Low	18	50.0	78.22
TOTAL	96	34.7	85.08

99 as given by Wechsler Intelligence Scale for Children adapted for Puerto Rico are, therefore, considered normal.

#### Average I. Q.

The average I. Q., as measured by W-Scale, of the ninety six children born of mothers in the oral group was 85.08 with a standard deviation of 13.7 while that of 114 children of the mothers in the non-oral group was 85.54 with a standard deviation of 11.4 (Table I). The difference of 0.46 points between the average I. Q. scores was found statistically non-significant (13). It was noted that the I. Q. score in the oral group ranged from a low score of 55 to a high of 133, while in the non-oral group it ranged from 54 to 118,

#### Age in Months and I. Q.

It is a prevalent notion among psychologists and other professionals such as educators that the I. Q. score changes with the age of the person. In our study group of 210 children the oral group consisting of 96 children had an average age of 73.3 months at the time of the measurement of I. Q. and the non-oral group with 114 children had an average age of 73.9 months (Table I).

There are no significant differences between average ages (in months) of the two groups nor between their average I. Q. scores. The correlation coefficients

between age and I. Q. for both groups did not differ significantly from zero, indicating that in the groups under study, the age did not have a significant effect on the I. Q. scores of the children.

#### Dosage, Socio-Economic Level and I. Q.

In many studies, the socio-economic conditions have been found to be related positively with educational and psychological indices of the school children (2).

In our experiment when the two groups, oral and non-oral, were compared in their socio-economic level scores (S.E.S.) the average socio-economic score of the mothers in the oral group was 3.18 (on scale of 0 to 7) while their children's average I. Q. was 85.08. The correlation coefficient between these two variables (S.E.S. and I.Q.) was 0.310, which is statistically significant.

In the non-oral group 114 children's data gave the average (S.E.S.) of their mothers as 3.31 and the average I. Q. was 85.54. The correlation coefficient between the two variables was 0.188 which is barely significant.

The tendency of relationship, as is found in such situations, indicates that the higher the socio-economic level the higher is the I. Q. score observed.

In order to study the effect of the dose of the pills taken by the mothers during their pre-pregnant period on the Intelligent Quotient (I. Q.) as measured by

TABLE III  
CORRELATION AND REGRESSION COEFFICIENTS ( UNIT EFFECTS) OF SIZE OF  
DOSE CONSUMED BY MOTHERS ON THE I. Q. OF CHILDREN BY SOCIO-ECONOMIC GROUP

Socioeconomic Group	Number of Cases	Coefficient of Correlation (r)		Unit Effect on I. Q. (b)	
Upper	12	-0.531	(NS)	-.1029	(NS)
Middle	66	-0.048	(NS)	-.0107	(NS)
Low	18	-0.078	(NS)	-.0108	(NS)
TOTAL -	96	-0.132	(NS)	-.0283	(NS)

(NS) Coefficient of correlation (r) and the effect (b) are not significant at 5 percent level.

Wechsler's Scale, it was decided to study the effect within three broad socio-economic groups of the patients (mothers) taking pills. Of the ninety six mothers of the oral group children in the experiment, twelve belonged to the upper level.

The difference between the average I. Q. of the lower socio-economic group and that of the upper and middle classes was found statistically not significant at the conventional probability level of 5 percent. (Table II). However, since in the lower class group more pills were consumed per mother than in the upper and middle class groups, the effect of the dose, if any, would be "confounded" with the possible effect of the socio-economic level; that is, the socio-economic level could conceivably mask the influence of the size of the dose. Therefore, since our prime purpose was to study the effect of the dose on the I. Q. score, a separate correlation estimate was worked for each of the three socio-economic groups.

The correlation coefficients in the three cases were negative all non-significant, indicating that the amount of contraceptive consumed by a mother before pregnancy is not related significantly with the I. Q. score of her child between 5 to 8 years of age in any of the three socio-economic groups. The correlation coefficient for the total of ninety six children, was minus 0.132, and the corresponding coefficient of linear

regression was 0. -0.0283 (Table III). The coefficient of correlation did not differ significantly from zero (at the 5 percent level) and hence it can be concluded that in general the effect of the dose on the I. Q. score is not significant, irrespective of the socio-economic class the mothers belong to. The unit effect of dosage on I. Q. is indicated by the regression coefficients (b) in the 4th. column of Table III. Since the correlation coefficients were not significant, they are not significant either.

### Summary

In this work we have presented the results of some parameters studied in a series of investigations on the possible effect on the intelligence quotient in offspring of oral and non-oral contraceptives users.

The data used for this study were obtained from a group of 210 children born to mothers who had used contraceptive methods (oral and non-oral) previous to pregnancy in a study group totalling 5,465 patients divided into two groups. We found the following results:

- (1) There was no significant difference between the intelligence quotients of the offspring

of the mothers in the oral group and the mothers in the non-oral group.

- (2) There was no difference between the average intelligence quotients of girls and boys of different ages.
- (3) There was no significant correlation between age and intelligence quotient in either of the two groups in the experiment.
- (4) There is a significant correlation between the socio-economic level and the intelligence quotient of the children in both groups.
- (5) In none of the three socio-economic groups (high, middle or low) we found a significant effect of the quantity of steroid contraceptive consumed by the mother on the intelligence quotient of her 5 to 8-year old child.

### Resumen

Se presentan en este trabajo los resultados de unos estudios de una serie de investigaciones sobre el posible efecto de los contraceptivos orales en la inteligencia de los niños nacidos a las madres que los usan previo al embarazo.

Los datos utilizados para este estudio provienen de 210 niños nacidos a madres que habían usado los métodos contraceptivos (oral y no-oral) previo al embarazo en un experimento con un total de 5,465 pacientes en dos grupos. Se encontraron los siguientes resultados:

- (1) No existe diferencia significativa entre el Cociente de Inteligencia de los niños de las madres del grupo oral y los de las madres del grupo no-oral.
- (2) No existe diferencia entre los Cocientes de Inteligencia promedio de los niños y niñas de distintas edades.
- (3) No existe correlación significativa entre la edad y el Cociente de Inteligencia en ninguno de los dos grupos en el experimento.
- (4) Existe correlación significativa entre el nivel socio-económico y el Cociente de Inteligencia de los niños en ambos grupos.
- (5) En ninguno de los tres grupos socio-económicos (alto, medio y bajo) se encontró efecto significativo alguno de la cantidad de esteroides contraceptivos consumida por la madre sobre el Cociente de Inteligencia de su prole.

### Acknowledgments

We gratefully acknowledge the helpful contribution of Senator Luis Izquierdo Mora, M. D., who made possible the assignment of special funds to the Maternal Health Program from the Puerto Rico Legislature, for our studies.

### References

1. *Abdul-Karim, R. W., Druker, M., Rizk, P.*: Influence of estrogen on the cholinesterase content of fetal brain. *Obstet. Gynecol.* 36: 5, 719-722, 1970.
2. *Bangdiwala, Ishver, S.*: Effect of socio-economic level on some educational factors in Puerto Rico, College of Education, University of Puerto Rico, Río Piedras, June, 1974.
3. *Bongiovanni, A., McPadden, A. J.*: Steroids during pregnancy and possible fetal consequences. *Fertil and Steril* 11: 181, 1960.
4. *Burstein, R., Wasserman, H. C.*: The effect of provera on the fetus. *Obstet. Gynecol.* 23: 6, 931-934, 1964.
5. *Churchill, J. A., Neff, J. W., Caldwell, D.*: Birth weight and Intelligence. *Obstet. Gynecol.* 28: 13, September, 1966.
6. *Dobbing, J., and Widdowson, E. M.*: The effect of undernutrition and subsequent rehabilitation on myelination of rat brain as measured by its composition. *Brain*, 88: 357, 1965.
7. *Drillien, D. M.*: The small for date infants: Etiology and prognosis. *Pediat. Clin. N. Amer.* 17: 9, 1970.
8. *Educational Research Center*: Socio-economic Scale by Ishver S. Bangdiwala and Antonio Alejandro Félix, a manual edited by Martha C. Rendon, University of Puerto Rico, 1970.
9. *Fuertes de la Haba, A., Bangdiwala, I., Pelegrina, I.*: Success of randomization procedure in a controlled contraceptive experiment. *Jour. Reprod. Med.* 11: 4, 142-148, 1973.
10. *Fuertes de la Haba, A., Curet, J. O., Pelegrina, I., Bangdiwala, I.*: Thrombophlebitis among oral and non-oral contraceptives users. *Obstet. Gynecol.* 38: 2, 259-263, 1971.
11. *Fuertes de la Haba, A., Curet, J. O., Pelegrina, I., Bangdiwala, I.*: Deaths among users of oral and non-oral contraceptives. *Obstet. Gynecol.* 36: 597-602, 1970.
12. *Fuertes de la Haba, A., Pelegrina, I., Bangdiwala, I., Hernández-Cibes, J. J.*: Changing patterns in cervical cytology among oral and non-oral contraceptive users. *Jour. Reprod. Med.* 10: 1, 3-10, 1973.
13. *Fuertes de la Haba, A., Santiago, G., Bangdiwala, I., Pelegrina, I., García, S.*: Intelligence Quotient in offspring of oral and non-oral contraceptive users. News Release, Medical Science Campus, University of Puerto Rico. May 30, 1974. Abstract published: *Medical World News A. McGraw Hill Publication.* 15: 36, 55-56, October 4, 1974.
14. *Roca, Pablo*: Problems of adapting intelligence scales from one culture to another. Puerto Rico Department of Education, Office of Evaluation, 1955.



## EL CONSENTIMIENTO INFORMADO MEDICO

Vicente Font-Zelinski, MD, JD

**H**ay un tipo de consentimiento no muy bien entendido precisamente por aquellos quienes deben obtenerlo, esto es los médicos. Se trata del consentimiento informado que debe dar el paciente al médico para que éste pueda llevar a cabo sus funciones como cirujano, como terapeuta o sus funciones de diagnóstico. Exclusivamente a este tipo de consentimiento va dirigido este artículo el cual esperamos sirva en algo para evitar confusiones tanto en el aspecto médico como en el aspecto legal. De producir más confusión que sirva entonces de estímulo a ambos campos, médico y legal y que al mismo tiempo levante inquietudes en ambos campos en cuanto a la forma de obtener el consentimiento informado y como expresarlo. Esto es de suma importancia específicamente para la clase médica ya que se trata de una acción en contra del médico muy poco usada por el demandante (paciente). Se presume la imparable proliferación en los próximos años de litigios en contra de los médicos en base a la acción de falta de consentimiento informado.

Las jurisdicciones federales en su inmensa mayoría aceptan que en este tipo de acción el demandante (paciente) no necesita ningún experto médico para probar su caso. Removiendo así uno de los obstáculos más grandes en el litigio por acciones de negligencia profesional contra el médico. Esta doctrina también se presume aplicará a otras profesiones tales como la de los abogados, los ingenieros, los arquitectos, etc.

Las nociones que en este artículo se exponen, no son indicativas del estado de cosas en Puerto Rico,

---

*Del Doctors Medical Center, Santurce, Puerto Rico.*

*Esta monografía se publicó en la Revista Jurídica de la Universidad Interamericana de Puerto Rico, Facultad de Derecho, Vol. X, Enero-Mayo 1976, Núm. 2. Del artículo original se suprimió la palabra "acometimiento", por no estar acorde con el nuevo Código Penal de Puerto Rico.*

pero sí resumen la línea de pensamiento en la mayoría de las jurisdicciones en los Estados de la Unión Americana. Sin embargo, podemos asumir que estos enfoques probablemente se presentarán en Puerto Rico en un futuro no lejano. La profesión médica y legal deben estar muy atentos al desenvolvimiento de esta doctrina de consentimiento informado por parte del paciente, ya que presentará otro problema más dentro de la llamada crisis de "mala práctica médica".

La doctrina del consentimiento informado proviene de la ley anglosajona del derecho común, que establece "la inviolabilidad del cuerpo humano".

Desde el punto de vista histórico, consideran algunos que la génesis de la doctrina del consentimiento informado, en Estados Unidos, tuvo lugar en el año 1914 en un caso en el estado de Virginia donde se demandó a un radiólogo. En este caso el radiólogo aplicó terapia de Rayos X a un paciente que padecía de una enfermedad de la piel. Este tratamiento era nuevo para aquella época. Hubo quemaduras y se demandó al radiólogo. El caso eventualmente fue a la Corte Suprema del estado de Virginia y el caso lo ganó el paciente-demandante bajo la doctrina de negligencia. Sin embargo en este caso (1914) la Corte Suprema de Virginia pronuncia un "dictum" que dice en términos generales, que el paciente no puede rendir un consentimiento a menos que se le explique inteligentemente lo relacionado a las complicaciones y que por lo tanto él tiene que estar en condiciones de "saber" lo referente a su tratamiento.

Hace años el eminente Juez Benjamín Cardozo, de la Corte Suprema de los Estados Unidos se manifestó en el sentido de que: "toda aquella persona adulta y en su sano juicio tiene el derecho a determinar que se hará con su propio cuerpo". Trece años más tarde otro eminente juez del mismo foro, el Juez Louis Brandeis amplió dicho concepto diciendo que: "los hacedores de la Constitución Americana buscaban proteger a los ciudadanos americanos en sus creencias, sus pensamientos, y en sus sensaciones. Confirieron el derecho

a que se les dejara en paz, uno de los derechos más básicos y más comprensibles”(1). O sea derechos fundamentales de todo ciudadano, enfermo o no.

### Aparente “Trasfondo”

La doctrina de falta de consentimiento informado por parte del paciente surgió con ímpetu a la luz pública a principios del 1973 cuando la Asociación Americana de Hospitales pidió a sus miembros la adopción de lo que ellos llamaron Declaración de Derechos de los Pacientes.

1. ....
2. ....
3. (El paciente tiene el derecho a recibir de parte de su médico, la información necesaria para poder dar su consentimiento informado, antes de dar cualquier comienzo a cualquier procedimiento o tratamiento (2) .....

Dos años más tarde, en el 1975, esa declaración ha sido fuertemente atacada inclusive por algunos miembros de la Asociación Americana de Hospitales, llamándosele “uno de los peores documentos del siglo XX”. La Asociación Médica de Puerto Rico adoptó también una Carta de los Derechos del paciente, prácticamente idéntica a la de la Asociación Americana de Hospitales excepto que la Asociación Médica de Puerto Rico suprimió la palabra “informado” cuando se refiere al consentimiento dado por el paciente.

1. .... 2. .... 3. .... 4. .... 5. .... 6. ....
7. “El paciente tiene el derecho a recibir de su médico toda la información necesaria antes de dar su consentimiento para cualquier procedimiento o tratamiento. Excepto en emergencias, dicha información debe incluir los riesgos médicos significativos envueltos y la probable duración de la incapacidad y no debe estar limitada necesariamente a un procedimiento o tratamiento médico específico. Donde existan alternativas médicas significativas para el cuidado o tratamiento o cuando el paciente las solicite, éste tiene el derecho a tal información. El paciente también tiene el derecho a conocer el nombre de la persona responsable de los procedimientos y/o tratamiento”. (3)

Por lo tanto, en la Carta de los Derechos del Paciente de la Asociación Médica de Puerto Rico no aparece

como un derecho del paciente “lo de consentimiento informado”.

En California la decisión en el caso de *Cobbs v. Grant* (4) abre las puertas para litigios a base de la falta de dar consentimiento informado por parte del paciente. Es de esperarse que en los próximos cinco años los litigios por dicha causa asciendan progresivamente, ya que sabemos que bajo esa acción no es necesario en la inmensa mayoría de los casos que el paciente presente peritos médicos. Decisiones como ésta al igual que los pronunciamientos de la Asociación Americana de Hospitales (véase Carta de Derechos) y Asociaciones Médicas locales (véase Carta de Derechos) en cuanto a los derechos del paciente, engendran al médico una responsabilidad enorme en el sentido de obtener consentimiento informado. Responsabilidades que le han sido descargadas al médico muy serias y que éste debe tener presente, entender y enfrentarse a ellas.

A pesar de la promulgación de la Carta de Derechos del paciente de la Asociación Médica Americana la jurisprudencia norteamericana, en términos generales acepta que un hospital no es responsable, ni aparentemente tiene tan siquiera la obligación, de que a un paciente se le informe adecuadamente acerca de su operación o tratamiento (5) ni tampoco tiene los medios fiscales para que se implemente dicha doctrina de consentimiento informado por parte de su facultad médica, por lo tanto es obvio que la responsabilidad recae enteramente sobre el médico a cargo del caso.

### Generalidades

Hay diferentes formas de consentimiento y autorizaciones para tratamiento, u operaciones quirúrgicas o procedimientos de diagnósticos dentro del campo médico. A grandes rasgos entendemos que el consentimiento a obtenerse en el caso de los adultos es diferente que para el caso de los menores. Que hay consentimientos, con implicaciones diferentes, para transplante de tejidos o transplante de órganos, etc. Hay consentimientos o autorizaciones para exámenes de autopsia, bien sean parciales o bien sean completas, al igual que hay otros tipos de consentimientos o autorizaciones tales como para las esterilizaciones, estudios investigativos, etc. También que hay formas de consentimiento usadas por muchos hospitales en el cual supuestamente el paciente da su consentimiento



to por escrito a un empleado clerical del hospital, pero la mayoría de éstas no tienen ninguna validez puesto que prácticamente lo que se hace es renunciar a negligencia futura a favor del hospital o del médico. También hay un consentimiento implícito en aquellos casos de emergencia, (de verdaderas emergencias) en aquellos casos en que es necesario la extensión de la operación o el tratamiento, por el bien del paciente. Es necesario entender que en estas situaciones de extensión de la operación se asume el consentimiento implícito ya que un nuevo consentimiento no sería posible, por ejemplo en el caso en que, el paciente está bajo anestesia, y es necesario hacer una extensión de la operación porque la situación surge imprevista. Debemos entender que no todas las extensiones dentro de la misma operación se deben considerar implícitas.

## **El Consentimiento Informado**

Para obtener un consentimiento informado del paciente debe el médico entender que desde el punto de vista legal éste debe informarle al paciente en forma que éste entienda sobre la naturaleza de su enfermedad, la razón, las alternativas y los riesgos a la operación, tratamiento o procedimiento de diagnóstico, propuestos por el médico no importa que el paciente pida dicha información o no. Salvo algunas excepciones tales como la incompetencia tanto de edad o mental, las emergencias verdaderas, etc. Otra excepción sería la de respetar el pedido por parte del paciente a que no se le informe sobre esos detalles.

A este respecto el departamento legal de la Asociación Médica Americana aconseja que una de las mejores defensas para evitar una acción de acosechamiento o una acción por falta de consentimiento informado de parte del paciente es la siguiente:

1. "Informarle al paciente de todos los hechos pertinentes en su caso y en un lenguaje que él entienda".
2. "Luego que éste firme un formato cuidadosamente fraseado indicando que él, el paciente, entiende lo que se le dijo".
3. "Que firme dicho formato en la presencia del médico preferiblemente, y con uno o más testigos cuando se le esté haciendo la explicación.
4. "Siempre que las circunstancias lo permitan es-

tos consentimientos deben obtenerse en la propia oficina del médico. También es permisible el que el mismo paciente escriba en las hojas de seguimiento del expediente médico del hospital, el hecho de que consiente al tratamiento u operación según sea el caso, que entiende claramente, y que le han sido explicadas las complicaciones y procedimientos alternativos". (6).

Autoridades médico-legales entienden que para un médico no es necesario bajo ciertas circunstancias obtener un consentimiento escrito para todas las fases del tratamiento. Con procedimientos rutinarios en la oficina el riesgo a ser demandado es en realidad tan poco que se justificaría en estas circunstancias descansar en el consentimiento implícito. Sin embargo, señalan que para cualquier procedimiento en el hospital o un procedimiento no usual en la oficina se debe conseguirse el consentimiento informado y por escrito del paciente. Es conveniente recordar que el consentimiento que obtenemos del paciente generalmente en nuestra comunidad puede ser anulado o quedar sin efecto bajo las siguientes circunstancias:

1. Porque el acto a que se consiente es en contra de la ley.
2. Porque el consentimiento fue dado por una persona que no tiene capacidad legal para darlo.
3. Porque no sea un consentimiento informado. (?)
4. Porque ha sido dicho consentimiento obtenido al hacer una representación errónea al paciente.
5. Por fraude.

El fraude es raro, sin embargo, la "falsa representación" no lo es. Por ejemplo, representarle, por vía de información, a un paciente que su operación o que determinado tratamiento es necesario para salvarle la vida o para preservar o para mejorar su salud cuando en realidad no hay base sólida para dichas afirmaciones y sobre todo cuando hay alternativas de tratamiento. Esto es representar falsamente y no hay consentimiento. También se ven en otros casos cuando se le representa la paciente que el tratamiento a ofrecérsele proporcionará mayor alivio que bajo cualquier otra alternativa. Estas situaciones vician el consentimiento dado por el paciente, no sólo el consentimiento expreso o implícito, sino también el consentimiento informado si se obtuvo bajo esa falsa presentación.

Muchos médicos desconocen el deber fiduciario de informarle a su cliente todo lo concerniente a su caso para poder obtener de éste, un consentimiento

informado. Un deber fiduciario en este caso se interpreta por el hecho de que las personas envueltas, en este caso el médico y el paciente, no están en un mismo nivel, uno está en desventaja de conocimiento. Por lo tanto, uno tiene más información y más conocimiento sobre la materia que el otro. Por lo tanto, resalta el deber fiduciario del médico para con su paciente.

Hasta aquí entonces todos nos estaremos preguntando qué debemos y cómo informarle al paciente y qué debe contener un consentimiento informado. En verdad existe una gran confusión no sólo para los médicos sino también para los Tribunales. Y se debe a que todavía no hay una forma adecuada de obtener y expresar un consentimiento informado para el paciente. Los expertos se han manifestado en el sentido de que ya es hora, e imperativo, de que los hospitales y las facultades médicas de los hospitales pidan y obtengan una participación mucho más activa de los asesores legales para que éstos aconsejen en estos asuntos.

La mayoría de peritos en aspectos médicos legales parecen estar de acuerdo en que los consentimientos informados deben contener por lo menos en términos generales una mención de los siguientes puntos:

1. La forma debe implicar claramente que al paciente se le hizo saber de la naturaleza de su enfermedad, los riesgos inherentes en la operación o en el tratamiento, las alternativas a dichos tratamientos tanto positivas como negativas y las alternativas a las operaciones o tratamientos.
2. Este consentimiento por escrito debe autorizar al doctor a usar su propio y mejor criterio médico de presentarse alguna condición inesperada, sobre todo en cuanto a extensión de las operaciones.
3. Debe indicarse que el médico no ha garantizado una cura. Esto a muchos les parecerá muy obvio y trivial. Sin embargo algunas autoridades insisten en que esto debe ponerse en dicho consentimiento ya que no son infrecuentes los casos en que el demandante pueda alegar, como así lo ha hecho en muchísimas ocasiones en corte, que el médico sí le prometió y sí le garantizó una cura. En estos casos volvemos al problema de qué credibilidad le dará el Tribunal a los envueltos en el caso.
4. Este consentimiento escrito debe también incluir y hacer constar el derecho que tiene el médico a usar un asistente o a usar otros médicos en cualquier momento (7).

Los puntos arriba expuestos usualmente son los puntos básicos para el cirujano o el terapeuta de práctica común y corriente en Hospitales de la Comunidad, no implica investigadores, etc. Los anestesiólogos tienen responsabilidades y obligaciones que atañen a su campo en particular, tanto dentro como fuera de la sala de operaciones y por lo tanto deben ser cubiertos éstos, o bien por un párrafo añadido a esa forma de consentimiento informado o bien sea redactando ellos mismos una forma para obtener consentimiento informado del paciente. Lo último es lo más prudente, pues de no hacerlo así el anestesiólogo tendría que descansar en un consentimiento informado obtenido por otra persona, con las posibles consecuencias que esto implica.

Hay otras áreas donde los consentimientos son diferentes y en estos mencionamos las salas de emergencia, las unidades de cuidado intensivo, las unidades coronarias, etc. Se necesita en estas dependencias, en muchos casos, de dicho consentimiento informado, sin embargo, en estas áreas, de presentarse una emergencia verdadera no es necesario conseguir el consentimiento ni informado ni por escrito. Simplemente procederá el médico a tratar dicha emergencia verdadera. Es bueno señalar que bajo estas circunstancias el médico debe asegurarse de que sí se trata de una emergencia verdadera para poder obviar el tener que obtener dicho consentimiento.

En el caso de los niños, tratándose de una emergencia, se debe actuar con la prontitud que amerita el caso, sin embargo todas las diligencias posibles deben ser realizadas, si el tiempo así lo permite para comunicarse y explicar la situación a los padres del niño o menor o al tutor o familiar más cercano del niño. En los casos de emergencia las cortes ven con mucha simpatía el que se le haya dado tratamiento médico adecuado y de emergencia aun en aquellos casos en que no se obtuvo el consentimiento.

## Las Acciones

Sin el consentimiento del paciente para su tratamiento (salvo las excepciones usuales), sea cual fuere, puede haber un cargo de agresión. Sin el consentimiento informado del paciente puede haber un cargo de agresión, o de negligencia, de acuerdo a distintas jurisdicciones, sin embargo, la doctrina que parece prevalecerá en los casos médicos en que no medie un consentimiento



informado será la doctrina de negligencia.

Para beneficio de la clase médica, debemos revisar algunos conceptos de estos dos términos, esto es, agresión y negligencia. Todos están familiarizados con el concepto de agresión en cuanto al derecho penal se refiere. En el derecho civil en Puerto Rico las obligaciones que nacen de culpa o negligencia están comprendidas en el Artículo 1802 del Código Civil 1930. Dicho artículo lee como sigue:

“el que por acción u omisión causa daño a otro, interviniendo culpa o negligencia, está obligado a reparar el daño causado. La imprudencia concurrente del perjudicado no exime de responsabilidad, pero conlleva la reducción de la indemnización” (31 L. P. R. A. 5141)

El elemento intención implica una actuación voluntaria de parte del demandado como lo es en agresión. Sin embargo, el elemento de intención está comprendido dentro del concepto de “culpa” en el artículo 1802 o sea, este concepto de culpa del artículo implica un elemento de intención o actuación voluntaria por parte del demandado.

La intención, para los efectos de la responsabilidad, desde el punto de vista del derecho civil por actos torticeros no tiene que ser necesariamente una hostil ni un deseo de causar daño, lo importante es que se produce un resultado que invade los derechos del demandado y por lo tanto no es necesario entonces que se trate de una intención maliciosa u hostil para que venga obligado a responder el demandado. Lo que en realidad implica es la presencia de un elemento de voluntariedad. En Puerto Rico uno de los casos típicos de agresión es el caso de Rojas v. Maldonado, 68 D.P.R. 818 (1948). En este caso lo importante es que los padres no habían autorizado el contacto del médico que lo operó, se había dado permiso a otro médico. Por lo tanto hubo agresión. Si el niño hubiera sido operado por el doctor al que se le dió el consentimiento y por ende autorizado a operar al niño no habría agresión; posteriormente de haber surgido una acción sería cuestión de probar negligencia.

El caso de Torres Pérez v. Hospital Doctor Susoni, 95 D.P.R. 867, (1968) establece la doctrina de que en caso de emergencia o cuando el comunicarle a la persona la necesidad de intervención pueda causarle mayor daño emocional no es necesario su consentimiento para llevar a cabo la operación. Este caso trata de la amputación de una extremidad.

Se expuso anteriormente que si se trata de una emergencia verdadera aun en un paciente adulto en

sano juicio y capaz de consentir, aun así el médico debe proceder a tratar la emergencia verdadera, sin embargo, hoy a la luz de la doctrina moderna de “consentimiento informado”, es sumamente peligroso desde el punto de vista legal proceder a una operación no autorizada por el paciente adulto y en su sano juicio si no se obtiene un consentimiento informado, aunque sea una emergencia verdadera. En lo que se refiere a la situación de empeorar o no la condición emocional del paciente, el médico debe estar avisado para que en su día presente prueba eficaz, sobre el estado emocional del paciente en esa situación y si actuó bajo esa situación sin el consentimiento informado.

En el caso de Montes v. Fondo del Seguro del Estado, 87 D.P.R. 199, (1963), “el practicar una intervención quirúrgica en una persona sin su consentimiento si bien técnicamente puede considerarse como un acometimiento y agresión no constituye el delito de acometimiento y agresión culpable por el código penal por carecer de elemento existente de intención”. La opinión mayoritaria en las jurisdicciones americanas nos indican lo que se expone en el caso de Montes v. Fondo del Seguro del Estado, supra, sin embargo, esta opinión mayoritaria le añade, que si bien no constituye un delito de agresión sí constituye un elemento de negligencia por parte del médico si no obtuvo el consentimiento informado. Por lo tanto debemos recordar que “intención” desde el punto de vista civil y a los efectos del Artículo 1802 del Código Civil, es en la “culpa” que encontramos el elemento de intención.

Nos inclinamos a pensar que en Puerto Rico tan pronto la esencia de esta doctrina del consentimiento informado llegue al entendimiento del paciente y su abogado, proliferarán las acciones por negligencia contra el médico en aquellos casos en que el consentimiento no haya sido obtenido adecuadamente. Es bueno señalar que en el caso de Oliveros v. Abreu, M.D. y Doctor's Center, Inc. (8) el Tribunal Supremo hace mención al hecho de que ya en Puerto Rico no se necesitarán expertos médicos para que el demandante pueda traer y prevalecer en su caso contra el médico en aquellos casos de “mala práctica médica”.

#### Algunas Opiniones de Tribunales Norteamericanos

Veamos ahora la jurisprudencia norteamericana en

cuanto a ciertos aspectos de este problema. Cuando hablamos de riesgos de operación, riesgos de tratamientos o riesgos de procedimientos de diagnósticos o sea riesgos que se le deben informar al paciente para que éste pueda hacer una decisión por sí mismo estos riesgos han sido descritos como "razonablemente previsibles" (9); y también como riesgos "sustanciales o materiales" (10).

En relación a cuanto se le debe informar al paciente, las opiniones mayoritarias y las minoritarias no difieren mucho. Básicamente difieren en cuanto a qué peso se le debe dar a lo que es "aceptable dentro de la comunidad médica". La opinión minoritaria sugiere que muy poco o en nada debe considerarse a lo que los médicos llaman "buena práctica de la medicina", ya que esto se interpreta en la mayoría de los casos como para ventaja propia (self-serving). La opinión minoritaria coincide con la mayoritaria en el sentido de que la prueba para determinar si un riesgo en particular debe ser informado al paciente, lo determinante debe ser: "si es material o no, o sea la materialidad para la decisión inteligente del paciente". Sin embargo la opinión minoritaria añade y cree que todos los riesgos potenciales que puedan afectar la decisión del paciente deben serle informado a éste. Por ejemplo, el hecho de que en determinada operación haya un factor riesgo de solamente 1 por ciento de una parálisis, así debe serle informado al paciente. La opinión mayoritaria cree que no es necesaria tanta divulgación si el procedimiento es simple y los riesgos "remotos y aceptados como tales". (11)

Lo usualmente aceptado para divulgación en pacientes temerosos puede tornarse en un arma de dos filos. Se ha aceptado por muchas jurisdicciones e inclusive por la opinión mayoritaria que el médico puede limitar su información de riesgo operatorio o de riesgo de tratamiento en un paciente que él considera suspicaz y que por lo tanto la divulgación podría empeorar su condición emocional (12).

Aquí es bueno apuntar que en algunas jurisdicciones norteamericanas se ha sostenido el hecho de que el médico que este justificado en no divulgar todos los riesgos envueltos en ciertos procedimientos al paciente no necesariamente tiene que hacer una divulgación completa al cónyuge (13). Sin embargo, el refrenarse de hacer ciertas divulgaciones a pacientes que uno considera temeroso debe ser constatada en el record médico sin lugar a duda y con suma cautela ya que este paciente una vez llega a juicio probablemente se convierta en el paciente menos suspicaz que ese médico jamás haya visto.

También se ha sostenido el hecho de que no importa que el paciente sea ansioso o temeroso, si los procedimientos a llevarse a cabo tienen una incidencia alta de reacciones adversas o complicaciones de naturaleza seria, aun así no importa el estado emocional del paciente, debe ser informado por completo (14).

En cuanto a la relación causal, la opinión mayoritaria promulga la doctrina de que esta relación surge cuando el paciente puede establecer, que de haber sido informado adecuadamente, no hubiera consentido al tratamiento (15). Obviamente ésta será una de las alegaciones del paciente-demandante, sin embargo, y afortunadamente para el médico, esta alegación del paciente-demandante debe ser establecida sin lugar a dudas en juicio.

Se acepta como prueba objetiva lo siguiente: "el qué hubiese decidido una persona prudente y razonable en la posición del paciente de haber sido adecuadamente informado de todos los riesgos envueltos" (16).

En cuanto a la naturaleza y el grado de riesgo se puede presentar la siguiente interrogante: ¿si el médico que le propone a un paciente determinada operación o determinado procedimiento de diagnóstico o tratamiento médico, sería éste negligente, si dejare de informar a sabiendas de que durante el curso de dicha operación, de dicho tratamiento o de dicho procedimiento, él no tendrá a su disposición métodos ideales de diagnóstico o personal adecuado para tratar con ciertas emergencias que surjan inesperadamente, por ejemplo, como lo sería un colapso cardio-respiratorio? Creemos que el caso de *Oliveros v. Abreu, M. D., Doctor's Center, Inc.* (17) al establecer la nueva forma en Puerto Rico para los casos de "mala-práctica" médica ayudaría a resolver la interrogante desde el punto de vista positivo. Creemos que sería negligente el médico en los hechos expuestos anteriormente si son del conocimiento propio del médico, esto es, si dentro de esa comunidad médica, se sabe que el personal que debe intervenir con esas emergencias serias no es adecuada para atender esas situaciones.

Otro ejemplo donde creemos que el médico podría ser hallado negligente sería el siguiente: cuando un médico, por cualquier medio, da a entender al paciente respecto a la experiencia, habilidad o pericia para llevar a cabo ciertos procedimientos o para llevar a cabo ciertos tratamientos, éste está expuesto a una acción por negligencia de encontrarse probado que no tiene esa experiencia que alega o da a entender



que tiene.

El caso de Scott v. Wilson (18) no debe interpretarse restrictivamente como que se aplica solamente en los casos de una "rpimera experiencia". Al contrario un médico puede repetir consistentemente un tratamiento sin tan siquiera haber tenido, ni tener, la pericia o entrenamiento adecuado para tal procedimiento y ser negligente si causa daño. Por lo tanto la defensa de la "experiencia" tan frecuentemente utilizada por la parte demandada en caso de pleitos de "mala-práctica" médica, puede ser una defensa sumamente vulnerable.

Ahora bien, qué tipo de acción podría traerse contra el médico en aquellos casos en que no hay un consentimiento informado o no se le haya explicado aquellos aspectos de "importancia material" en cuanto al tratamiento médico, complicaciones, etc., y al cual el paciente tiene derecho a saber. Al presente en la mayoría de las jurisdicciones norteamericanas hay dos teorías para este problema. La teoría de la negligencia y la teoría de la agresión. Sabemos que casi todo contacto sin consentimiento por parte de una persona contra otra puede dar lugar a una acción de agresión. En los Estados Unidos el caso Shetter v. Rochelle (19) expone la teoría de agresión en casos que envuelven tratamiento no autorizado. A continuación lo que se expuso en el caso:

"It seems to be well established that if a doctor operates upon a patient without his patient's consent, that he has committed a battery upon the patient and is liable in damages therefore. If the consent given to the operation in question was ineffectual, every phase of this operation was a continuing battery for which recovery should be allowed, even if the operation has been successful."

Casos claros y típicos de agresión, son aquéllos en que, por ejemplo:

- A. El paciente consiente a una operación de estómago; se le hace la operación y además se le hace una operación de tiroides para la cual no hubo consentimiento informado.
- B. El paciente consiente para una operación de la próstata y sus cordones espermáticos sufren daño y no se le informó de esa posibilidad.
- C. Los casos en que por ejemplo se efectuó

mielograma o un estudio artereográfico sin haberle informado adecuadamente sobre los riesgos de dicho procedimiento y hay una complicación con consecuencias mayores. Por ejemplo, en el estudio artereográfico sufre un accidente cerebro-vascular.

Estos son casos obvios en el cual la teoría de agresión impera y no hay necesidad de demostrar negligencia o malicia. El demandante será indemnizado por los daños sufridos debido a procedimientos no autorizados aun cuando la operación o procedimiento hayan sido ejecutados perfectamente. Recordemos que los elementos tradicionales de violencia o intención de hacer daño están ausente de plano en la mayoría de los casos de "mala-práctica"; se suplementan por la "culpa" del Artículo 1802.

La teoría de agresión obviamente se reserva para aquellos casos en que el paciente no ha consentido claramente al procedimiento efectuado en dicho paciente (20). Bajo estas circunstancias el requisito de una intención deliberada se sustituye por la "desviación del consentimiento dado por el paciente", y por lo tanto una causa de acción por agresión está presente (21).

La Corte Suprema de California (sabemos tiene una fuerte persuasión sobre otras jurisprudencias inclusive la de Puerto Rico) por un "dictum" se ha manifestado en el sentido de que cuando se da tratamiento a un paciente que ha consentido y surge una complicación de la cual no se habló, pero que tiene un porcentaje bajísimo como complicación en ese procedimiento, California se ha manifestado en el sentido de que no ha habido una desviación del consentimiento. Que en estos casos el médico faltó en su obligación de informar al paciente todo lo pertinente al caso, complicaciones, etc. Bajo estas circunstancias le llama una acción por negligencia (22).

Sin embargo es bueno recordar que la teoría aplicable a estos casos de consentimiento informado no es totalmente clara por completo, o sea, no se ha llegado a una decisión unánime en cuanto a qué acción debe invocarse, si la acción de agresión o si la acción de negligencia o ambas acciones. Todo parece indicar, y el criterio de la mayoría así lo deja ver, que estas acciones se consideran como negligencia (23).

Es interesante notar que en algunos casos las compañías de seguros han intentado eludir su responsa-

bilidad en pleitos alegando que la acción por falta de consentimiento informado es uno de agresión y el médico queda, si esta acción de las compañías de seguro progresa, huérfano totalmente de la protección de su póliza. Afortunadamente, las cortes se han resistido a este subterfugio por parte de los aseguradores. En el caso de *Shehee v. Aetna Casualty and Surety Co.* (24) se le dijo a la compañía que no. Que independiente de que al médico se le olvidó obtener el consentimiento informado aun así, no se trataba de agresión y sí de "mal practice", que sí estaba cubierta por la póliza en cuestión.

### Resumen

Hasta hace unos cuantos años en muchas de las jurisdicciones en los Estados Unidos cuando el paciente sufría una lesión como consecuencia de una complicación en ciertos procedimientos de diagnóstico u operaciones, esos casos se veían en corte como casos de negligencia contra el médico. Por lo tanto, el paciente tenía que traer peritos médicos para probar la negligencia del médico demandado y como es de conocimiento general esto era, y es, sumamente difícil de conseguir.

Sin embargo, en los últimos años en los Estados Unidos han aumentado las acciones en contra de los médicos por éstos no informar "inteligentemente" al paciente sobre la condición a tratar, el método o tratamiento, y las alternativas y complicaciones de dicho tratamiento. Por consecuente surge una acción por la doctrina de falta de consentimiento informado por parte del paciente. En Puerto Rico creemos que estas acciones por falta de consentimiento informado del paciente aparecerán muy pronto. Sobre todo en esta era de consumerismo en la que vemos a diario que aquél que consume está empeñado, y así debe ser, en saber cómo, cuándo, por qué y cuánto. La profesión médica y paramédica no es una excepción, no escapa de las inquietudes del consumidor en este aspecto. Por lo tanto hoy en día estamos viendo que el paciente pretende, exige y espera en la gran mayoría de los casos que se le explique todo lo concerniente a su tratamiento médico. El consentimiento informado debe ser obtenido por el médico de cabecera o mejor por el médico que intervenga en la manera más directa con el procedimiento, tratamiento u operación a realizarse en el

paciente.

Para el médico es de suma importancia obtener correctamente dicho consentimiento informado ya que es bueno recordar que en este tipo de acción donde se alega por parte del paciente-demandante que no ha sido informado debidamente no se necesita que dicho paciente traiga prueba pericial médica; por lo menos en la mayoría de las jurisdicciones en los Estados Unidos. Hay varias excepciones a la necesidad de las reglas de consentimiento informado por parte del paciente, una de las excepciones es una emergencia, otra excepción es en el caso de un menor o un incapacitado para consentir donde corre peligro su vida de no actuarse inmediatamente, y algunas otras.

Sin embargo, es bueno recordarle al médico que al levantar la defensa de una emergencia, posteriormente de surgir una acción, hay que probarla como tal y sin lugar a duda. En muchos casos las alegaciones de emergencia al ser vistas en su fondo resultan no ser del tipo de excepción a esta regla. O sea, resulta ser emergencia "no verdadera". Y qué resulta ser una emergencia no verdadera? Por ejemplo: operar apresuradamente un paciente en el que se sospecha apendicitis sin un previo período razonable de observación. El dolor abdominal resulta no ser debido a una apendicitis sino a una condición trivial que no requería intervención. Sin embargo, como consecuencia de la operación se desarrolla un absceso o una fístula. Obviamente no había emergencia verdadera en operar apresuradamente.

¿Qué debe el médico informar al paciente? Mucho. Y cómo debe informárselo es punto de debate entre ambas profesiones tanto la médica como la legal. En el campo médico se sigue la línea de pensamiento de que hay ciertas complicaciones que siendo muy raras o que pudieran asustar al paciente hasta el grado de que éste no permita el tratamiento o la operación siendo ésta sumamente necesaria, pues, que estas complicaciones no deben mencionársele al paciente. ¿Cómo cuáles? Complicaciones realmente no muy frecuentes como lo es un paro cardíaco durante la operación, como lo es una embolia pulmonar durante o después de la operación, o como lo es un infarto del miocardio durante o después de la operación. La profesión médica alega que este sería llevar al ánimo del paciente ansiedades y preocupaciones realmente innecesarias.

En el campo legal, en la inmensa mayoría de los casos, se adopta la posición de que todas las complicaciones, alternativas al tratamiento, u operacio-



nes, riesgos inherentes al procedimiento o al tratamiento deben ser informados al paciente en forma "inteligente" que quiere decir: informarle lo suficiente para que éste pueda rechazar o aceptar dicha operación o dicho tratamiento en caso que así lo juzgue necesario o conveniente para él.

En algunas jurisdicciones de los Estados Unidos la corte ha propuesto que: una vez se traiga acción contra el médico y se alegue falta de consentimiento informado por parte del paciente la línea de pensamiento sería la siguiente: si habiéndosele informado a una persona prudente y razonable sobre las complicaciones (no a una persona como el paciente, sino a una persona de razonable entendimiento) si de habersele informado sobre esas complicaciones aun así esa persona de razonable intelecto o de razonable capacidad mental hubiera aceptado la operación o el tratamiento en particular. De ser así, de haberse aceptado por una persona prudente y razonable, la acción contra el médico se cae. De no ser así, esto es, si una persona prudente y razonable entiende la corte que hubiere rechazado el procedimiento médico aconsejado, prevalecerá la acción contra el médico.

Entonces debemos entender que aquel paciente que ha consentido adecuadamente es un paciente a quien el médico le ha impartido suficiente información médica pero sin tecnicismos y en lenguaje que él pueda entender. Información acerca de su tratamiento, operación o procedimiento de diagnóstico para que éste pueda hacer una decisión inteligente al respecto en cuanto a si debe proceder o no con dicho tratamiento. El médico por su parte al solicitar un consentimiento adecuado debe entonces informar razonablemente sobre los peligros dentro de su conocimiento cuales fueren, incidentales o posibles en dicho tratamiento o intervención que se propone. Aclaremos que cuando se refiere a *dentro de sus conocimientos* es necesario recordarle a la clase médica que ese conocimiento bajo la nueva doctrina que establece el caso de *Oliveros v. Abreu, M.D., y Doctor's Center, Inc.* es sumamente abarcadora. Se revocó la norma de la comunidad y se implantó la nueva forma que es la siguiente: "Aquella que, reconociendo los modernos medios de comunicación y enseñanza, establece que el nivel o calidad de esa atención debe ser la que llena las exigencias profesionales generalmente reconocidas por la profesión médica. Lo dicho en *Rivera v. Dunscombe* (25) en el sentido de que 'un médico sólo viene obligado a dar a sus pacientes aquella aten-

ción médica que generalmente se emplea para casos similares por el resto de los médicos en la comunidad,' queda revocado por ser incompatible con la norma que aquí adoptamos". (26).

## Conclusiones

En Puerto Rico no tenemos aún jurisprudencia sobre consentimiento informado. Creemos que de presentarse este tipo de acción nuestro Tribunal se inclinará, como hace la opinión mayoritaria en los Estados Unidos, en el sentido de que a menos que se encuentre ante un caso tan patéticamente obvio de agresión, el caso usual de falta de consentimiento informado lo considerará como una acción de negligencia.

Al no necesitarse perito médico por la parte demandante se abren las puertas para la proliferación de esta clase de litigio. Creemos que esta doctrina de falta de consentimiento informado se presentará en litigio en mayor número tan pronto el paciente esté consciente de la disponibilidad de dicha defensa. Nos atrevemos a implicar que en algunos casos será más fácil que probar *Res Ipsa Loquitur*.

Por lo tanto la profesión médica debe ir en busca de sus asesores legales para que les instruya sobre esta nueva y grave responsabilidad del médico. Creemos que los asesores legales de los hospitales y de las facultades médicas de cada hospital deben entrar de lleno en este asunto, dándole así la protección a la profesión médica, que ésta necesita.

## Referencias

1. *Bower, Derby Trout*. The Malpractice Plague. Number No. 3, Medical Economics Cassette Service, Medical Economics Company, Oradell, New Jersey, 1973.
2. Declaración de Los Derechos de Los Pacientes, Asociación Americana de Hospitales.
3. Carta de Derechos de los Pacientes, Asociación Médica de Puerto Rico.
4. *Cobbs v. Grant* 8 Cal. 3d 229, 104 Cal. Rptr. 505, 502 P. 2d. 1 (1972).
5. *Florentino v. Wenger*, 19 N. Y. 2d 407, 280 N. Y. S. 2d 373, 227 N. E. 2d 296 (1967). Véase *Schloendorff v. Society of New York Hosp.* 211 N. Y. 125, 105 N.E. 92 (1914)
6. *Hassard, H.*, Medical Malpractice: Risks, Protection, Pre-

- vention, Medical Economics Book Division, Inc., New Jersey, 1966.
7. *Ibid.*
  8. 101 D.P.R. 209 (1973)
  9. *Mason v. Ellsworth*, 3 Wash. App. 298, 474 P. 2d 909 (1970) (perforation of esophagus during esophagoscopy was not "reasonably foreseeable").
  10. *Mallet v. Pirkey*, 171 Colo. 271, 466 P.2d 466 (1970).
  11. *Cobbs v. Grant*, *supra*.
  12. *Salgo v. Leland Stanford Jr., University Board of Trustees*, 154 Cal. App. 2d 560, 317 P.2d 170 (1957) (court held instruction on duty of physician to disclose should include statement that physician has such discretion in the case of an apprehensive patient.)
  13. *Nishi v. Hartwell*, 52 Haw. 188, 473 P.2d 116 (1970). Unless disclosure is necessary for the care of protection of the patient, a physician has no legal obligation to inform a patient's family concerning his treatment. The idea that physician has a responsibility to reveal all to the family is not based on law, but on an ethical duty to consider the feelings of the patient's loved ones. Also, it has been said to be "good public relations," and, in some instances, the general discussion between the physician and family following the disclosure is helpful to the physician in selecting the best method of therapy.
  14. *Starnes v. Taylor*, 272 N.C. 386, 158 S.F.2d 339 (1968).
  15. *Cobbs v. Grant*, *supra*.
  16. "Since at the time of trial the uncommunicated hazard has materialized, it would be surprising if the patient-plaintiff did not claim that had he been informed of the dangers he would have declined treatment. Subjectively he may believe so, with the 20/20 vision of hindsight, but we doubt that justice will be served by placing the physician in jeopardy of the patient's bitterness and disillusionment." *Id.* 104 Cal. Rptr. at 515. Véase *Canterbury v. Spence*, 464 F. 2d 772 (1972).
  17. 101 D.P.R. 209 (1973).
  18. *Scott v. Wilson*, 396 S.W. 2d 532 (Tex. Civ. App. 1965), *affd.* 412 S.W. 2d 299 (Tex., 1967) (physician led patient to believe he was experienced in performing stapedectomy operations when in fact it was his first such operation on a live patient: his experience had been with cadavers).
  19. *Shetter v. Rochelle*, 2 Ariz. App. 358, 409 P.2d 74 (1965), modified 2 Ariz. App. 607, 411 P.2d 45 (1966).
  20. *Wilkinson v. Vesey*, 295 A.2d 676 (1972).
  21. *Cobbs v. Grant*, 8 Cal. 3d 229, 104 Cal. Rptr. 505, 502 P.2d 1 (1972).
  22. *Id.*, 104 Cal. Rptr. at 512.
  23. *Prosser, W. L.*, Handbook of the Law of Torts, 4th ed., p. 165, West Publishing Co., St. Paul, Minnesota, 1971.
  24. *Shehee v. Aetna Cas. & Surety Co.*, 122 F. Supp. 1 (W.D. La., 1954).
  25. 73 D.P.R. 819, 838 (1952).
  26. 101 D.P.R. 209, 226 (1973).



# EPIDEMIOLOGIA DE HONGOS ATMOSFERICOS EN PUERTO RICO -PARTE I

Carlos López-Almodóvar, MD

La incidencia de rinitis y asma bronquial en Puerto Rico es significativa a juzgar por el volumen de pacientes afectados que vemos anualmente en nuestras clínicas ambulatorias. La morbilidad de estos pacientes en toda la isla nunca se ha estimado pero se correlaciona con las cifras de Estados Unidos de América o tal vez sean mayores (6-7 por ciento de la población total). La identificación y cuantificación de esporas de hongos alergénicos en la atmósfera se ha correlacionado con la descompensación de pacientes afectados por rinitis alérgica y asma bronquial (5). Las diferencias reportadas entre estudios de hongos atmosféricos en Norte América con otros afines en nuestra isla, posiblemente guarda relación con las diferencias climatológicas (4). De igual forma, aquellos estados que forman parte del Golfo de México y disminuyen menos las diferencias climatológicas con las islas del Caribe, tienden a tener una prevalencia de hongos atmosféricos parecidos a la nuestra (4, 6, 7).

La prevalencia de una humedad relativa alta y un promedio de temperatura alrededor de los 80° F, durante todo el año, hace de Puerto Rico e islas adyacentes un lugar propicio para la proliferación de hongos atmosféricos todo el año. Estudios previos al nuestro, (1, 2, 3), despiertan nuestro interés para emprender un estudio epidemiológico por etapas de los hongos atmosféricos y sus posibles repercusiones clínicas en

pacientes afectados por rinitis alérgica y asma bronquial.

1. Si ocurren fluctuaciones estacionales significativas en la flora de hongos atmosféricos en P. R.
2. El efecto de las variaciones climatológicas en la cantidad de esporas de hongos atmosféricos.
3. Cómo el presente estudio compara con otros estudios previos de hongos atmosféricos en la isla en cuanto a la incidencia de los diferentes géneros.

## Procedimientos y Métodos

Placas esteriles de cultivo conteniendo agar-saburoud fueron expuestas en una plataforma especial localizada en el tercer piso (azotea) del Hospital de Veteranos en San Juan. La plataforma movable era adecuadamente orientada en contra de la dirección del viento durante cada período de exposición sin ser afectada por extractores de gases, reflectores, chimeneas, etc. El tiempo de exposición fue alrededor de las 2:00 pm cada lunes y martes desde febrero de 1971 hasta enero de 1972. Dos placas fueron expuestas por cinco minutos y otras dos por 15 minutos durante cada día de exposición. Un total de ocho placas fueron enviadas por correo aéreo al Laboratorio de Micología de la Universidad de Oklahoma para aislamiento e identificación (8).

La identificación, el aislamiento y el conteo de colonias fueron hechas alrededor del quinto día después de la exposición en el Laboratorio mencionado bajo la supervisión del Dr. Glenn S. Balmer, Ph. D.

De acuerdo a la prevalencia alrededor de 12 meses corridos, se distinguen cuatro grupos en orden descendente:

## Objetivos

Los objetivos de este estudio fueron el determinar:

**TABLA I**  
**PORCENTAJE DE COLONIAS IDENTIFICADAS DE HONGOS ATMOSFERICOS ENTRE**  
**FEBRERO DE 1971 A ENERO DE 1972. FUERON EXCLUIDOS LOS CULTIVOS QUE NO**  
**ESPORULARON**

---

1. Cladosporium	19.63
2. Aureobasidium (Polullaria)	16.43
3. Yeast (Candida, Cryptococcus, spp.)	14.08
4. Penicillium	11.71
5. Curvularia	13.02
6. Monilia	11.71
7. Aspergillus	6.42
8. Alternaria	2.44
9. Helminthosporium	2.44
10. Cephalosporium	.74
11. Epicoccum	.74
12. Phoma	.56

---

A. Grupo que suman un 50 por ciento

1. Cladosporium
2. Aureobasidium
3. "Yeasts"

B. Grupo que suma el 36.44 por ciento

1. Curvularia
2. Penicillium
3. Monilia

C. Grupo que suma 11.30 por ciento

1. Aspergillus
2. Alternaria
3. Helminthosporium

D. Grupo que suma 2.26 por ciento

1. Cephalosporium
2. Epicoccum

### Discusión

La poca variación climatológica a través del año en la isla de Puerto Rico no hace diferencias marcadas en la incidencia de hongos atmosféricos. Las variaciones en temperatura en la Costa Norte de la isla oscila de 71° F a 92° F y la humedad relativa oscila de 58 por ciento a 64 por ciento. Algunas noches la humedad relativa alcanza un máximo de 75 por

ciento. Si esto favorece la esporulación más rápida y la saturación de esporas en el aire alcanza un porcentaje mayor con el aumento de humedad y temperatura, puede explicarse que este sea uno de los factores que descompensan la rinitis alérgica y el asma bronquial durante la noche en pacientes alérgicos a hongos atmosféricos.

La leve fluctuación en algunos géneros durante el año puede estar relacionada directamente con los cambios de humedad relativa ya que existe en la isla un período lluvioso y otro relativamente seco.

Los hallazgos de Pons-Belaval se asemejan a los nuestros en cuanto a asignarle un papel preponderante a Cladosporium sobre todos los demás géneros. Coincide también con el nuestro en la incidencia intermedia aproximada de "Yeasts" y Penicillium. También se parece la descripción minoritaria del género Aspergillus.

Difiere el informe de Pons-Belaval con el nuestro en cuanto al género Nigrospora que ellos le asignan un papel secundario importante y apenas nosotros pudimos identificar ese género. En cambio, nosotros le asignamos un papel secundario pero destacado a Aureobasidium y Pons-Belaval lo relega a último lugar. Nuestros hallazgos en el género Curvularia fueron probablemente más elevados que el estudio previo mencionado. Las posibles variaciones pueden explicarse en base de una diversidad de lugares de exposición que utilizaron Pons-Belaval. Pueden también

**TABLA II**  
**A CONTINUACION SE COMPARA LA INCIDENCIA DE LOS HONGOS ATMOSFERICOS**  
**MAS ABUNDANTES ENCONTRADOS EN NUESTRO ESTUDIO CON EL QUE INFORMO**  
**PONS-BELAVAL EN LOS AÑOS 1958 Y 1961. SE TOMA ESTE ESTUDIO PORQUE SE**  
**ASEMEJA AL NUESTRO EN LUGAR Y TIEMPO DE EXPOSICION (2)**

Pons-Belaval 1958	Pons-Belaval 1961	López-Almodóvar 1971-72
1. Cladosporium	1. Cladosporium	1. Cladosporium
2. Nigrospora	2. Nigrospora	2. Aureobasidium
3. Yeasts	3. Penicillium	3. Yeasts
4. Penicillium	4. Phomopsis	4. Curvularia
5. Fusarium	5. Yeasts	5. Penicillium
6. Aspergillus	6. Phoma	6. Monilia
7. Curvularia	7. Aspergillus	7. Aspergillus
8. Ustilago	8. Fusarium	8. Alternaria
9. Stemphylium	9. Aureobasidium	9. Helminthosporium
10. Aureobasidium	10. Helminthosporium	10. Epococcum

haber ocurrido pequeñas discrepancias en la identificación del género.

### Conclusión

El género *Cladosporium* (*Hormodendrum*) se encuentra en la atmósfera en la ciudad de San Juan en una proporción de 20 por ciento en relación a los géneros saprofitos que esporulan. La cifra compara favorablemente con los hallazgos de la Costa del Pacífico en Estados Unidos (6, 7, 8), y con estudios hechos en la isla en 1959 y 1961 (2).

Encontramos que *Aureobasidium* (*Pulullaria*) le sigue en abundancia con un 16.43 por ciento, siendo notable que este género se encuentra abundantemente mezclado con el polvo, en los closets, cortinas de baños, fregaderos, (donde hay acumulación de sarro y grasa).

Al preparar las soluciones de extractos de hongos para hiposensibilizar a los pacientes de rinitis y asma bronquial, no solo debe tomarse en cuenta el historial y positividad de reacciones cutáneas a hongos atmosféricos, sino la proporción en la atmósfera de los mismos y el grado de antigenicidad del género.

Finalmente, la correlación de hongos atmosféricos que encontramos dentro de las viviendas merece ser estudiada en un futuro cereano en nuestro medio ambiente.

### Summary

A 12 month survey of airborne fungal spores was conducted in San Juan, Puerto Rico. Two major groups composed 86.44 percent of the total population were identified. Scattered seasonal variation of the different genera were observed. Our study correlates well with other studies completed in the San Juan area and with other reports from the U. S. Gulf Shore. More specificity in the hyposensitization procedures with allergenic fungi is the goal of these series of studies. Correlation with the indoor mold growth is being done at the present time.

### Reconocimientos

El autor tiene una deuda de gratitud con Dr. Leo H. Crip,

Profesor Emérito de la Universidad de Pittsburgh y con Dr. Glenn S. Balmer, Director del Laboratorio de Micología de la Universidad de Oklahoma por la contribución científica y financiera al presente estudio.

### Referencias

1. *Toro, Rafael*: Studies on the Aerobiology of Puerto Rico, *Journal of Agriculture of the University of Puerto Rico*, 30: 97-101 (1946).
2. *Pons, E. R., Jr. & Belaval, M. E.*: The Importance of Fungus Spores as Airborne Allergens in Puerto Rico. *Boletín Asociación Médica de Puerto Rico*, (Vol. 50, No. 1, 1958).
3. *Roure, Luis A., & Ramírez, José M.*: The Fungi which Caused Allergic Rhinitis and Bronchial Asthma in Mayagüez, P. R.; *Caribbean Journal of Science*, Vol. 10, 384 (1970).
4. *Collier, T. W. & Ferguson, B. A.*: Airborne Fungus Spores, Brunswick, Ga., Area - Incidence and Variation with Climatic Changes, *Annals of Allergy* 11: 480-493, 1953.
5. *Morrow, Lowe and Prince*: Mold Fungi in the Etiology of Respiratory Allergic Disease; *Journal of Allergy* 13: 215-226, 1941.
6. *Prince and Meyer*: An Up-to-Date Look at Mold Allergy, *Annals of Allergy*, July 1970.
7. *Stalker and Moore*: Airborne Pollen and Fungus Spore Patterns in the Birmingham, Alabama Area; *Annals of Allergy*: 30: 326-344, 1972.
8. Airborne Fungi from Five States in the Continental U. S. And Puerto Rico, *Annals of Allergy*, September 1974; Sorenson, Balmer, and Criepe.



$\frac{20}{150}$

# H

$\frac{20}{100}$

# EAR

$\frac{20}{70}$

# ING IS

# AS PRECIOUS

# AS SIGHT HAVE

# YOU HAD YOUR HEARING

# TESTED LATELY A SIMPLE

# COMFORTABLE HEARING

# INVESTMENT OF A FEW MINUTES

Hearing losses are among the most consistently neglected health problems. Many

people with them won't even admit it to themselves, let alone others. A little encouragement may

start them thinking about themselves more realistically.

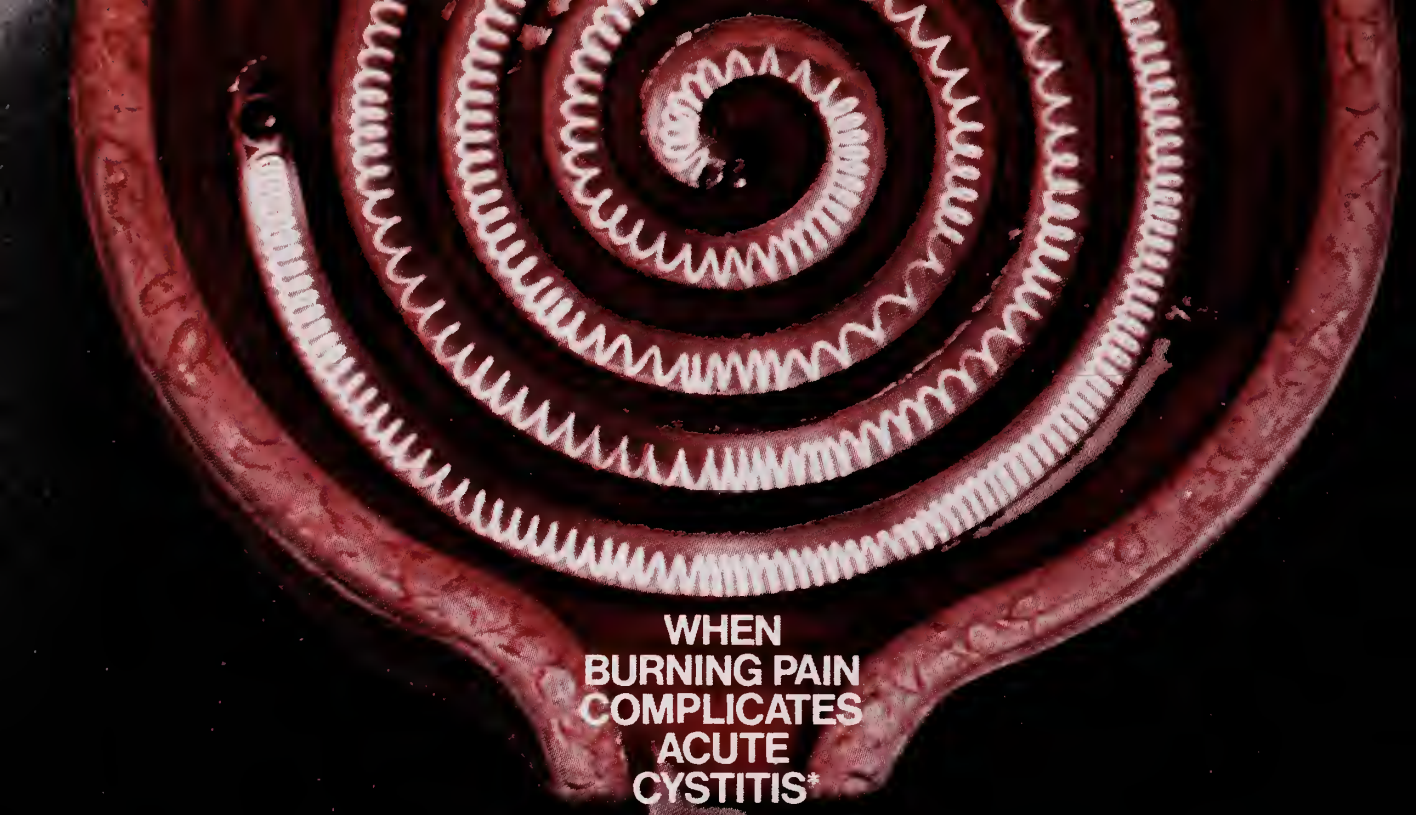
That's why we're offering you the poster shown here. You can hang it on the wall or stand it on a small table. It comes with booklets called "As

precious as sight" that give your patients some basic facts about auditory testing and hearing losses and how easy they are to correct in many cases.

Write to us for your free poster and booklets. They just might help you to help some patients who aren't hearing as well as they used to. Even those who ordinarily wouldn't hear of it.

Professional Relations Division, Beltone Electronics Corporation  
4201 West Victoria Street, Chicago, Illinois 60646, an American company

***Beltone***  
WHEN A HEARING  
AID WILL HELP



WHEN  
BURNING PAIN  
COMPLICATES  
ACUTE  
CYSTITIS\*

TURN IT OFF WITH

# AZO GANTANOL<sup>®</sup>

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

## FOR THE PAIN

- Quickly relieves painful symptoms such as burning and pain associated with urgency and frequency.
- Recommended antibacterial therapy: up to 3 days with Azo Gantanol, then 11 days with Gantanol (sulfamethoxazole).

## FOR THE PATHOGENS

- Effectively controls susceptible pathogens such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

\*nonobstructed: due to susceptible organisms

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies.

**Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura

hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); G.I. reactions (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

**Dosage:** Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**NOTE:** Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



# DYAZIDE<sup>®</sup>

Each capsule contains 50 mg. of Dyrenium<sup>®</sup> (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

Trademark

## MAKES SENSE FOR LONG-TERM CONTROL OF HYPERTENSION\*

**LOWERS  
BLOOD  
PRESSURE**

**CONSERVES  
POTASSIUM**

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### **\* WARNING**

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**\* Indications:** When the fixed combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium-sparing action of its 'Dyrenium' component is warranted.

**Contraindications:** Further use in progressive renal or hepatic dysfunction; hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs. Routine use of diuretics in otherwise healthy pregnancy.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with

cardiac irregularities. It is more likely in severely ill patients with urine volume less than one liter/day, the elderly or diabetics, with suspected or confirmed renal insufficiency. Periodic determinations of serum K<sup>+</sup> should be made. If hyperkalemia develops, substitute a thiazide alone, restrict K<sup>+</sup> intake. The presence of a widened QRS complex or arrhythmia in association with hyperkalemia requires prompt additional therapy. Thiazides are reported to cross the placental barrier and appear in breast milk; fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and other adverse reactions that have occurred in the adult may result. When used in pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics, or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K<sup>+</sup> frequently; both can cause K<sup>+</sup> retention and elevated serum K<sup>+</sup>. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium<sup>®</sup> (triamterene, SK&F Co.), and

leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Do periodic blood studies in cirrhotics to check for nondrug-related variations in blood pictures, and in patients with folic acid depletion, since 'Dyrenium' may contribute to appearance of megaloblastosis. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

**Adverse Reactions:** Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

**Supplied:** Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

**SK&F CO.,** Carolina, P.R. 00630  
Subsidiary of SmithKline Corporation

## TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE



**BURROUGHS WELLCOME CO. MAKES  
CODEINE COMBINATION PRODUCTS.  
YOU MAKE THE CHOICE.**



**EMPIRIN<sup>®</sup>  
COMPOUND  
c̄ CODEINE  
#3**

Each tablet contains:  
codeine phosphate, 32 mg (gr ½),  
(Warning: May be habit-forming);  
aspirin, 227 mg; phenacetin, 162 mg;  
and caffeine, 32 mg.



**EMPRACET<sup>™</sup>  
c̄ CODEINE  
#3**

Each tablet contains:  
codeine phosphate, 30 mg (gr ½),  
(Warning: May be habit-forming);  
and acetaminophen 300 mg.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



## EL CONSENTIMIENTO INFORMADO MEDICO: ANALISIS, DEFENSA, Y OPINION

*La necesidad de proteger los derechos civiles del ser humano obteniendo un consentimiento informado para cualquier procedimiento diagnóstico o terapéutico es de vital importancia tanto para el paciente como para el médico. En el artículo que acompaña esta edición, el Dr. Font-Zelinski da a conocer de una forma sucinta y somera el peligro que atraviesa un médico al hacer funciones de cirujano o terapeuta sin informar detalladamente al paciente el procedimiento al cual se somete. Tomando en consideración que hoy en día la mayoría de los médicos catalogan de trivial el obtener un consentimiento informado, ya por estar abrumado de trabajo o no tener el tiempo disponible para explicarle en detalle al paciente los procedimientos y sus consecuencias, no es de dudar que el paciente tiene una gran ventaja sobre el médico para demandar por acción de negligencia. Esta ventaja se acrecenta aún mucho más cuando reconocemos y sabemos que actualmente la práctica de la medicina se hace muy difícil por la gran salva de conocimientos científicos que diariamente surgen y el médico ignora o no los puede asimilar al mismo paso que aparecen. Como consecuencia, el médico se hace susceptible a cometer errores de juicio o de ignorancia y surge el factor de iatrogenia. De esta susceptibilidad se aprovecha el Dr. Iván Illich en su controversial libro Némesis Médica y hace eco de alarma acusando a los médicos de provocar enfermedades o situaciones adversas a la salud del hombre. El Dr. Illich indudablemente no reconoce que muchas de las llamadas enfermedades iatrogénicas no surgen de la ignorancia del médico sino del milieu inherente del individuo que lo hacen susceptible a ciertas reacciones adversas, como lo es una sensibilidad a drogas provocadas por deficiencias enzimáticas. En estos casos el médico usualmente no tiene los elementos de juicio a priori para evitar este problema y sería esotérico el hacer decenas de pruebas enzimáticas para pronosticar una reacción que es sumamente rara. Es claro que esta situación, así como otras, no eximen al médico de la responsabilidad profesional y el punto vital que levanta el Dr. Font-Zelinski e implica el Dr. Illich es que la responsabilidad principal del médico es el de informar al paciente de todas y cada una de las consecuencias del procedimiento diagnóstico o terapéutico. Aunque sea una situación muy rara y se haya reportado solamente una o dos veces en la literatura es el deber del médico informarle al paciente que dicha reacción puede ocurrir. En otras palabras, los médicos tenemos que realizar que estamos siendo obligados a practicar medicina defensiva, aunque no sea muy honorable.*

*Uno de los campos donde ha proliferado el requerimiento de un consentimiento informado médico detallado es el de la investigación. Hospitales donde se hacen investigaciones que envuelven seres humanos se han visto obligados a crear comités que guardan por sus derechos civiles. Al imponerse este requerimiento por las distintas agencias gubernamentales continentales se creyó que las exigencias impuestas causarían una animosidad del paciente hacia el médico en no aceptar el riesgo de someterse a una situación experimental. Como investigador clínico he sido testigo de múltiples sorpresas en este respecto ya que la incorporación de pacientes a estudios de investigación no ha declinado con el consentimiento informado. Más importante aún, la gran mayoría de pacientes que se someten a investigación han aceptado totalmente la franqueza del médico por este tipo de información detallada.*

*¿Cuál es entonces la problemática que existe? Algunos médicos no explican nada para no alterar al paciente, otros explican poco, otros delegan en la enfermera, otros explican solamente lo trivial y no enfatizan los detalles importantes, algunos no hablan con franqueza de las consecuencias por temor a ser rechazados por el paciente y finalmente otros explican detalladamente pero no lo documentan en el expediente clínico del paciente.*

*Ante esta situación el Dr. Font-Zelinski suscita la siguiente pregunta: ¿qué debemos los médicos informar al paciente? En mi opinión la respuesta sería: TODO. La franqueza no puede excluir nada. Me explico: debemos informarle al paciente que entre los efectos adversos pero sumamente raros de un medicamento se encuentran desde la caída total del cabello hasta paro cardíaco que provoque la muerte. Así también debemos informarle todas las situaciones imprevisibles que pueden acontecer por una intervención quirúrgica. No solamente se debe informar al paciente sino también a la familia que en muchas ocasiones son los demandantes.*

*Es importante también que las instituciones hospitalarias donde se llevan a cabo los procedimientos diagnósticos o terapéuticos tomen parte activa en requerir un consentimiento informado ya que los litigios abarcan tanto al médico como a la institución. Idealmente, y desde el punto de vista defensivo, este consentimiento debe ser específico para cada procedimiento y no usar una forma universal para cada procedimiento. Se debe elaborar un consentimiento informado para una operación de vesícula, uno para tiroide, etc. Un comité de la institución debe en todo momento fiscalizar el uso apropiado de los consentimientos informados.*

*Es preciso observar que el problema es ubicuo. El médico debe mantenerse informado al día en el aspecto académico. Los cursos de educación médica continua nos ayudan grandemente a abolir el factor de ignorancia que consecuentemente lleva a la iatrogenia. La comunicación y diálogo paciente-médico es sumamente esencial para evitar litigios. La franqueza, sinceridad y positividad del médico no deben ser escollo a esta relación y no pueden acarrear malos resultados. Los hospitales se deben mover a crear un interés más genuino hacia el problema del litigio profesional. Ya es hora también que la Asociación Médica de Puerto Rico tome riendas y guíe a los médicos y juristas a resolver este gran problema. Resuelto este problema podríamos pronosticar que los litigios contra médicos serán menos frecuentes y los costos exorbitantes de los seguros de responsabilidad médica van a declinar precipitosamente.*

José L. Cangiano, MD

## HEW NEWS:

The Department of Health, Education, and Welfare today proposed regulations which would permit a provider of Medicare services to request a change of intermediary at any time during the cost reporting year.

Intermediaries are health insurance organizations, such as Blue Cross plans and commercial insurance companies, that administer Medicare hospital insurance under contracts with the government. Current regulations require 120 days' notice of change prior to the end of a provider's fiscal year. The new provision removes the 120-day requirement and permits changes during the cost reporting year.

Experience has shown that the present requirements are unduly restrictive and could prevent changes of intermediary that would be in the best interests of Medicare.

Interested parties have 45 days after today's publication in the Federal Register to submit comments.

---

Beginning January 1, 1977, the maximum amount of earnings in a year that count for social security will automatically increase to \$16,500, up from this year's maximum of \$15,300, James B. Cardwell, Commissioner of Social Security, announced today.

Also in 1977, the maximum amount that a beneficiary can earn and still get all his social security checks will increase to \$3,000 in a year under the same automatic increase provisions of the law, Commissioner Cardwell said. The 1976 figure is \$2,760.

People who earn more than \$3,000 in 1977 may still get some social security benefits, but every two dollars they earn above \$3,000 may cause a reduction of one dollar in their social security benefits for the year. No matter how much they earn in 1977, they can get their full benefit for any month in which they do not earn more than \$250 in wages (up from \$230 in 1976) and do not perform substantial services in self-employment.

The Commissioner noted that these increases are determined on the basis of a formula in the law which automatically produces a result based on reported wage statistics.

"The formula is designed to keep both the contribution and benefit base, and the retirement test exempt amount, up to date as average wage levels rise throughout the Nation."

Commissioner Cardwell said. "Under the law, these automatic increases can take effect only after a year in which there has been an automatic increase in social security benefits." This requirement was met by a 6.4 percent automatic increase in benefits that took effect earlier this year.

The contribution and benefit base is the maximum amount of earnings in a year that are creditable toward social security benefits and are taxable under social security. The new base of \$16,500 will provide additional income to the social security program without increasing the taxes of workers who earn \$15,300 or less in a year, the Commissioner said.

He noted that the social security tax rate, now at 5.85 percent of taxable earnings for employees and employers each, and 7.9 percent of taxable earnings for self-employed people, will remain unchangeable in 1977.

The increase in taxes payable on 1977 earnings for workers who earn more than \$15,300 will range up to a maximum of \$70.20 each for a wage earner and his employer, and \$94.80 for a self-employed person. The maximum social security tax a wage earner will pay in 1977 will be \$965.25, and a self-employed person \$1,303.50.

An estimated 19 million workers—about one out of six covered by social security—will be affected by the increase in 1977 because they will have earnings of more than \$15,300. The increase in the base will result in additional taxes of \$2.3 billion on 1977 earnings.

"In return for the increase in taxes," the Commissioner said, "these affected workers will have greater protection because a larger amount of their earnings will be credited toward benefits than before. This will mean higher benefits for them and their families in the event of retirement, disability, or death, than would have been possible without an increase in the base."

About 1.3 million beneficiaries will receive additional benefits as a result of the increase to \$3,000 in the retirement test exempt amount in 1977. Additional benefit payments for 1977 will amount to an estimated \$150 million, the Commissioner said.

---

## AMA NEWS RELEASE:

"FREE BLEEDERS" WARNED TO AVOID ASPIRIN



CHICAGO— There are many drugs that cause increased bleeding in anyone inclined to be a "free bleeder," and the most common of these is aspirin, says a report in the Feb. 9 issue of the Journal of the American Medical Association.

Aspirin causes little bleeding problem for most individuals, but those who are likely to bleed easier and more freely than most should cause it, says Emily E. Czapek, M. D., of Children's Memorial Hospital and Northwestern University Medical School, Chicago.

Both physicians and patients should be made aware of this situation, so that those with bleeding problems can avoid aspirin and use a substitute, says Dr. Czapek.

Aspirin is found in many non-prescription products, she points out.

A satisfactory substitute is acetaminophen, says Dr. Czapek. This drug will help control discomfort and pain without increasing the hazard of bleeding.

Dr. Czapek writes in an editorial in the Journal, to accompany a research report by C. Harold Mielke, Jr., M. D., and colleagues from the Pacific Medical Center, San Francisco. Dr. Mielke reports on a study confirming that acetaminophen causes no increase in bleeding time, but that aspirin causes a significant increase in those prone to bleed freely.

"Acetaminophen is an antipyretic (fever reducer) and mild analgesic (pain reliever) that may be useful when influence on hemostasis (bleeding) is undesirable," Dr. Mielke concludes.

#### INFANT DEATHS BLAMED ON FAULTY CRIB BEDS

CHICAGO— A new baby at your home? If so, throw away that old crib. And don't replace it with a used one borrowed or purchased from a relative or neighbor.

In the March 1 issue of the Journal of the American Medical Association Dr. Millard Bass of the Wayne County (Detroit, Mich.) Office of the Medical Examiners reports that 15 infants in Wayne County died during a 30-month period (Jan. 1973-June 1975) as a result of accidental suffocation or strangulation in their cribs. In some the head caught between the mattress and crib rail; some caught the head between bars of the crib rail; two were hung on the side of the mattress and a broken crib rail. Several strangled on pacifier strings, necklace or nightgown.

On the basis of the Wayne County deaths, Dr. Bass estimates that as many as 1,000 suffocation deaths may have occurred nationwide during the 20-month period, and "This represents a substantial preventable infant mortality."

The new regulations, worked out through cooperation of the government and the manufacturers, require (1) Cribs must be of a standard size so that the mattress will fit snugly; (2) Crib slats are not more than 2 3/8 inches apart; (3) A locking device on the drop rail must be secure from accidental opening; (4)

The drop-side panel must be at least nine inches above the mattress when it is lowered.

How can the family determine whether the crib is safe? The Michigan physician lists these points:

It is obvious that a good mattress should fit snugly at each corner of the crib. There is danger if the crib mattress has lost its resiliency after years of use. Lack of proper fit may occur when an undersized or unconventionally shaped crib mattress is used in a standard-sized crib. Parents should exercise great care in providing mechanical toys that are designed to be attached to crib rails. The drop side of the crib should be in good working order and should meet the federal specifications. A damaged or broken crib should be repaired promptly, or it should be destroyed.

#### MEDICAL GROUP PRACTICE CONTINUES TO GROW IN 1970S

CHICAGO— While a substantial portion of the nation's health care is still delivered by the solo practitioner, medical group practice continues to show significant growth in the 1970's.

This is a major finding of the 1975/76 edition of the American Medical Association's *Profile of Medical Practice*, published this summer. The book is the fifth in a series which provides reference data on the practice of medicine in the U. S., compiled by the AMA's Center for Health Services Research and Development from the AMA Physician Masterfile and from the AMA Periodic Survey of Physicians.

*Profile of Medical Practice* is published as a companion to *Socioeconomic Issues of Health*, a book containing updated information on the socioeconomic issues of health from a variety of sources outside the AMA.

*Socioeconomic Issues of Health* shows the steady increase in number of physicians in the United States. In 1950 there was a physician for each 711 Americans. In 1974 the figure was one physician for each 566 persons. Total number of physicians in 1974 was 379,748.

Today, there are 8,483 medical groups in the United States, whose 66,842 physicians represent 23.5 percent of the active non-federal physician population, the AMA studies find. Medical groups are also increasing in size as well as in number. If present trends continue, it is likely that the solo, fee-for-service practitioner will continue to decline in importance while group practice becomes more prevalent. The small-scale, single-specialty group of three to five physicians may well become the predominant choice of young physicians.

Other highlights of "Profile of Medical Practice" include:

- \* Municipal hospitals are devoting more resources to outpatient and emergency care and less to inpatients in the 1970s, and these trends most likely will continue into the 1980s. Many patients will continue to visit



emergency departments at hospitals for non-emergency health conditions.

- \* A review of the literature suggests that health care researchers generally agree that allied health workers can increase the physician's productivity. There appears to be important potential for delegation of many routine tasks by the physician.
- \* Economic controls, in effect from August, 1971, to April, 1974, appear to have had important impact on physician's incomes. For most specialists, evidence indicates that increases in practice expenses exceeded the rate of increases in fees, and that this has had a dampening effect on the rate of change in net incomes. Evidence also indicates that the rate of increase in net incomes may be returning to pre-control levels.
- \* There is wide geographic variation in physician's fees, ranging from \$6.49 for follow-up office visit in communities with less than 10,000 persons to \$17.01 for areas with populations over five million. Much of this variation is due to the specialty composition of the area.

*Socioeconomic Issues of Health* includes additional data on the growth of group practice from sources other than the AMA. Topics covered include the evolution of self-regulation in medical practice, economic factors affecting physicians location, primary care programs, geographic distribution of foreign medical graduates, federal programs to influence location of physicians, and a description of the National Health Planning and Resources Development Act of 1974.

**THYROID SUPPLEMENTS LINKED TO INCREASED BREAST CANCER RISK**

CHICAGO— Prolonged use of thyroid supplements seems to be related to increase of breast cancer, says a report in the Sept. 6 Journal of the American Medical Association.

In the study reported by Chandrakant C. Kapdi, M. D., and John N. Wolfe, M. D., of Hutzel Hospital, Detroit, it was found that incidence of breast cancer among patients receiving the thyroid supplement was 12.13 percent, while in a control group that were not taking the supplement the incidence was 6.2 percent.

Likelihood of breast cancer increased with the number of years on the thyroid supplement, up to 19.48 percent for those taking the substance more than 15 years. The incidence was higher among women who had never given birth.

In commenting on the report, William R. Barclay, M. D., JAMA editor, pointed out that most of the women taking thyroid supplements did not develop breast cancer.

Thyroid supplements are so essential for individuals with inactive or sluggish thyroid glands that physicians should continue to prescribe thyroid supplements when indicated but

with proper patient counseling regarding the risk, Dr. Barclay said.

Low thyroid output can lead to debilitating, serious health problems, unless corrected by supplements, he said.

**ASPIRIN SUBSTITUTE OVERDOSE IS NEW HEALTH HAZARD**

CHICAGO— Overdose of acetaminophen — the popular aspirin substitute for relieving minor pain and discomfort — can cause severe liver damage and even death, says a report in the Oct. 18 Journal of the American Medical Association.

Acetaminophen poisoning now represents one of the most common causes of hepatic (liver) failure in Britain. Because of increasingly widespread use of over-the-counter acetaminophen preparations, it is imperative that the clinician be aware of the potentially lethal consequences of overdosage.

In proper doses, acetaminophen is generally safe and useful and clearly is an acceptable alternative to aspirin, but in overdose it is highly dangerous.

Some trade names for acetaminophen are Amphenol, Apamide, Apap, Concetol, Datriol, Febrolin, G-1, G-Lixir, Nebs, Neopap, SK-Apap, Tempra, Tylenol, and Valadol.

**OBESITY RATHER THAN DIET BLAMED IN HIGH CHOLESTEROL**

CHICAGO— Reducing excess weight is the first approach to lowering cholesterol and other fats in the blood, rather than a diet that avoids foods high in cholesterol, a study reported in the Oct. 25 Journal of the American Medical Association found.

Allen B. Nichols, M. D., of the University of Michigan School of Medicine, Ann Arbor, and colleagues, studied virtually the entire adult population of Tecumseh, Mich., to determine the effect of diet and overweight on cholesterol and triglyceride levels in the blood. Consumption of 110 different food items, both high and low in fats and sugar, was tabulated for 4,057 adults. Levels of blood fats were measured.

The findings:

There was no significant association between serum lipid (blood fats) levels and the frequency of consumption of fat, sugar, starch, alcohol and tea for both men and women.

But serum cholesterol and triglyceride concentrations were significantly higher among men and women who were markedly overweight.

Elevated fats in the blood had long been associated with increased risk of heart disease and other health problems.

Other factors besides fat intake are determinants of cholesterol levels among the general public, says Dr. Nichols.

However, Dr. Nichols cautions that the apparent independence of dietary habits and serum lipid levels does not mean that

diet and lipid levels are unrelated. But the degree of obesity is more obviously related to serum levels than the particular diet.

## A N U N C I O


---

### SE RENTA PARA OFICINAS MEDICAS

Espaciosa casa moderna, 1,306 pies cuadrados, tres habitaciones con sus baños, estudio, sala y dos comedores independientes de habitaciones. Cocina con todo equipo moderno. Magnífica para oficinas grupo de médicos. Mejor sector de Hyde Park, Las 'Marías 226 - directamente detrás de Panificadora Pepín y el Hato Rey Plaza. Renta módica. Información 765-5091, 765-8488, Sra. A. Rojas.

### LISTA DE ANUNCIANTES

1. BELTONE ELECTRONICS	HEARING AIDS
2. BOEHRINGER INGELHEIN	TORECAN
3. BURROUGHS WELLCOME	CODEINE ANALGESICS, SEPTRA DS
4. EATON LAB.	MACRODANTIN
5. MERCK, SHARP & DOHME	ALDOMET
6. ROCHE LAB.	AZO-GANTANOL, BACTRIM, VALIUM
7. W. H. RORER	MAALOX
8. SMITH, KLINE & FRENCH	DYAZIDE
9. SYNTEX LAB.	NEO-MULL-SOY
10. U. S. V. PHARM.	HYGROTON



**"Little Boy Blue,  
come blow your horn,  
The sheep's in the  
meadow, the cow's  
in the corn..."**

Since cow's milk and corn are leading causes of food allergy among infants, NEO-MULL-SOY® formula doesn't contain either one. Other leading soy formulas do contain corn syrup. Next time recommend corn-free NEO-MULL-SOY formula first. Mothers like its milky whiteness. And now it's easier for them to find NEO-MULL-SOY formula, because it's more readily available at grocery and drug stores.



**NEO-MULL-SOY®**

Soy Isolate Formula

The only leading soy formula  
that's milk-free AND corn-free.

**SYNTEX**

SYNTEX LABORATORIES, INC.  
PALO ALTO, CALIFORNIA 94304



# Septtra<sup>®</sup> vs Nitrofurantoin

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazole

## A new clinical

### **Efficacy: A draw.**

By randomized assignment, 149 patients received two Septtra tablets b.i.d. and 140 received one 100 mg capsule of nitrofurantoin macrocrystals q.i.d. for 14 days. Eight days after therapy ended, 94% of patients treated with Septtra had a clear culture vs 90% of those treated with nitrofurantoin macrocrystals.<sup>1</sup>

### **Laboratory changes: A draw.**

There was no significant difference in the incidence of laboratory changes except in one instance; a significantly larger proportion of patients on nitrofurantoin macrocrystals had decreased lymphocyte counts than did patients on Septtra.<sup>1</sup> The significance of this change is not known. (For further details see page three of this advertisement.)

### **Clinical side effects: Advantage, Septtra.**

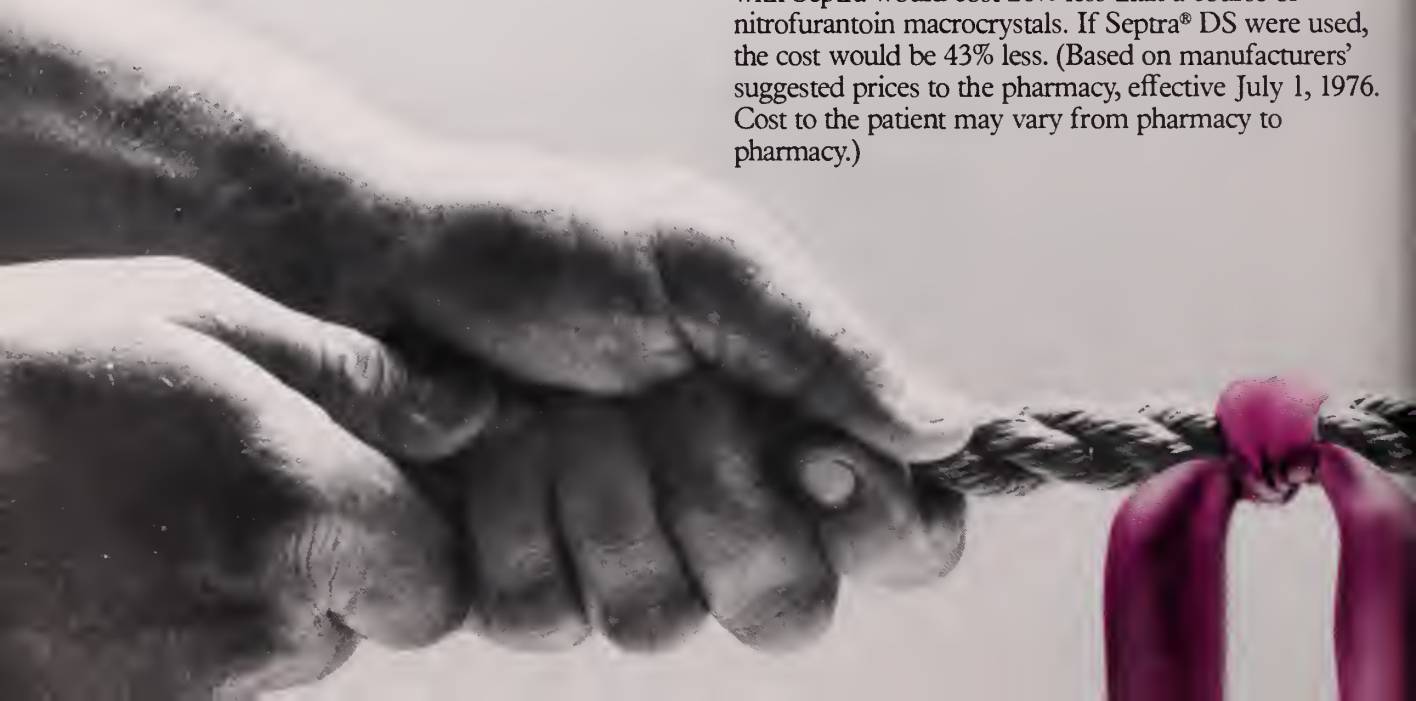
A significantly larger proportion of patients experienced side effects on nitrofurantoin macrocrystals (13%) than on Septtra (6%).<sup>1</sup> (For further details, see chart on page three of this advertisement.)

### **Convenience: Advantage, Septtra.**

To maintain effective antibacterial activity, Septtra is taken just twice a day, while nitrofurantoin macrocrystals are taken four times daily. The Septtra dosage schedule offers obvious advantages in terms of patient convenience and compliance.

### **Cost: Advantage, Septtra.**

At the dosages used in this study, a course of therapy with Septtra would cost 26% less than a course of nitrofurantoin macrocrystals. If Septtra<sup>®</sup> DS were used, the cost would be 43% less. (Based on manufacturers' suggested prices to the pharmacy, effective July 1, 1976. Cost to the patient may vary from pharmacy to pharmacy.)





# Nitrofurantoin

Macrocrystals

## Confrontation

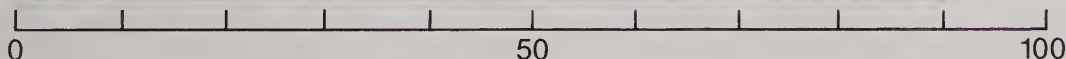
Results after 14-day course of therapy in 289 patients with recurrent urinary tract infections\*<sup>1</sup>

Septra

94%

Nitrofurantoin  
Macrocrystals

90%



% of patients with clear culture 8 days after therapy ended

\*Due to susceptible strains of *E. coli*, *Klebsiella*, *Enterobacter*, *Proteus mirabilis* and other *Proteus* species. Criterion for infection—100,000 or more organisms/ml urine. Criterion for “clear culture”—1,000 or fewer organisms/ml urine.

# Septra<sup>®</sup> DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

**Double Strength Tablets.**

**The most economical  
form of Septra.**



# Septra<sup>®</sup> vs Nitrofurantoin

Each tablet contains:  
80 mg trimethoprim and  
400 mg sulfamethoxazole

Macrocrystals

## Clinical side effects: Advantage, Septra.

## Laboratory changes: A draw.

Side effect	Frequency <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
nausea	3	16
vomiting	1	9
anorexia	1	4
abdominal pain	—	2
diarrhea	—	4
headache	2	—
dizziness	—	1
diaphoresis	1	—
pruritus	2	1
vaginitis	1	—
maculopapular rash	1	1
rash	—	2
urticaria	2	—
	14	40

**Note:** All patients who originally entered the study described on previous pages were included in the evaluation for clinical side effects (192 patients received Septra, 191 received nitrofurantoin macrocrystals). Some patients experienced more than one side effect. See **Adverse Reactions** section below for other reactions that may be encountered.

Type of change	Drug administered	
	No. patients with change/total patients tested <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
RBC ↓	14/141	14/141
Hemoglobin ↓	27/188	36/183
WBC ↑	3/188	3/183
" ↓	6/188	7/183
Bands ↑	3/183	3/176
" ↓	26/183	20/176
Hematocrit ↓	34/188	27/183
SGOT ↑	5/176	4/167
Basophils ↑	14/179	16/171
Neutrophils ↑	27/188	25/182
" ↓	3/188	6/182
Lymphocytes ↑	15/188	18/182
" ↓	11/188	21/182
Eosinophils ↑	14/179	8/177
Monocytes ↑	10/188	11/180
" ↓	23/188	23/180
Specific gravity ↑	1/187	—
" " ↓	—	1/177
Casts ↑	6/186	5/182
WBC/HPF ↑	9/190	13/185
RBC/HBF ↑	12/190	12/185
Bacteria ↑	9/189	11/183
" ↓	30/189	32/183
Crystals ↑	9/185	9/181

**Note:** Certain patients were not tested for some of the laboratory values listed above. Therefore, the chart specifies the total number of patients who completed the prescribed series of tests for each individual laboratory measurement.

**Indications:** Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37: 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. At present, data are insufficient to recommend use in infants and children under 12.

**Precautions:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria,

serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

**Supplied:** Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

Reference: 1. Data on file, Medical Department, Burroughs Wellcome Co.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



There is only one  
macrocrystal  
nitrofurantoin...  
and only Eaton  
has it.

Eaton

Consistent  
potency  
against the  
most prevalent  
uropathogens.

# Macrochantin<sup>®</sup>

(nitrofurantoin macrocrystals)

capsules 25mg 50mg 100mg



<sup>®</sup> EATON LABORATORIES  
Norwich International  
410 Park Avenue  
New York, N.Y. 10022  
U.S.A.

**INDICATIONS:** Indicated for the treatment of pyelonephritis, pyelitis, and cystitis due to susceptible *E. coli*, enterococci, *S. aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses) and certain strains of *Klebsiella-Aerobacter*, *Proteus* and *Pseudomonas*.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function, infants under one month, pregnant patients at term, known hypersensitivity.

**WARNINGS:** May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. (Such patients should be closely observed while receiving nitrofurantoin.) Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to *Pseudomonas*. Safety not established during pregnancy and lactation, should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.

**PRECAUTIONS:** Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal

impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**ADVERSE REACTIONS: Gastrointestinal Reactions**—Anorexia, nausea, emesis are the most frequent reactions, less frequently, abdominal pain and diarrhea, rarely, hepatitis. This dose-related toxicity reaction can be minimized by reduction of dosage, especially in the female patient.

**Hypersensitivity Reactions**—Pulmonary sensitivity reactions, which can be acute, subacute, or chronic. Acute reaction is commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on X-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and resolve with cessation of the drug therapy. Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation

of the drug therapy.

**Dermatologic Reactions**—Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other Sensitivity Reactions**—Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.

**Hematologic Reactions**—Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurological Reactions**—Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

**Miscellaneous Reactions**—Transient alopecia.

**SUPPLIED:** Macrochantin (nitrofurantoin macrocrystals) is available in opaque, yellow capsules of 100 mg (coded Eaton 009) and in opaque, yellow and white capsules of 50 mg (coded Eaton 008) in bottles of 30, 100, 500, and 1,000 capsules, and in opaque, white capsules of 25 mg (coded Eaton 007) in bottles of 100 capsules. Macrochantin Capsules, 50 mg and 100 mg, are also available in hospital unit-dose packages, strip-packaged in boxes of 100



# In hypertension



# Hygroton® 50 mg.

## (chlorthalidone)

### blocks sodium retention longer

*Diuretics reduce blood pressure by blocking sodium retention to lower "effective" volume. But the body's renal compensatory mechanisms are mobilized to promote a secondary sodium conservation, expand "effective" volume and perhaps reelevate blood pressure. Sustained control of "effective" volume is therefore essential to treatment. No other diuretic blocks sodium retention longer than Hygroton.*

### Provides sustained control

Since the effects of Hygroton are exerted over a 24-hour period, sodium diuresis is gradual and prolonged. At the renal tubular level, Hygroton thwarts attempts of the renin/angiotensin/aldosterone system to conserve sodium, thus keeping "effective" volume and blood pressure down. Inadequate doses of diuretics may permit the renin/angiotensin/aldosterone system to prevail, but Hygroton helps inhibit it through . . . a "24-hour sentry" effect

### Enhances patient compliance

The "24-hour sentry" effect of Hygroton allows once-a-day administration. This uncomplicated regimen encourages patient compliance through simplicity and economy. Proven efficacy and compliance have made Hygroton one of the most widely prescribed diuretic/antihypertensives for mild to moderate hypertension today.

# Hygroton®

## the 24-hour sentry

### For effective once-daily therapy

#### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone; routine use of diuretics in an otherwise healthy pregnant woman with or without mild edema is contraindicated and possibly hazardous. **Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May be additive or potentiative of the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Usage in women of childbearing age requires that the potential benefits of the drug be weighed against its possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in cord blood and breast milk. **Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis; dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia; purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg. (white, scored) and 50 mg. (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6.



USV Pharmaceutical Mfg. Corp.  
Manati, P.R. 00701



# Maalox®... on balance, it's better



- **more effective**—49% more acid neutralizing capacity than the next leading antacid.\*
- **greater patient acceptance**—over 25 years' experience with millions of patients.
- **less costly**—50¢ less per bottle than the next leading antacid.

- **less sodium**—36% less sodium than the next leading antacid.

Minty Maalox. Well tolerated, month after month...year after year.

\*per minimum recommended dose.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034



# BOLETIN ASOCIACION MEDICA DE PUERTO RICO

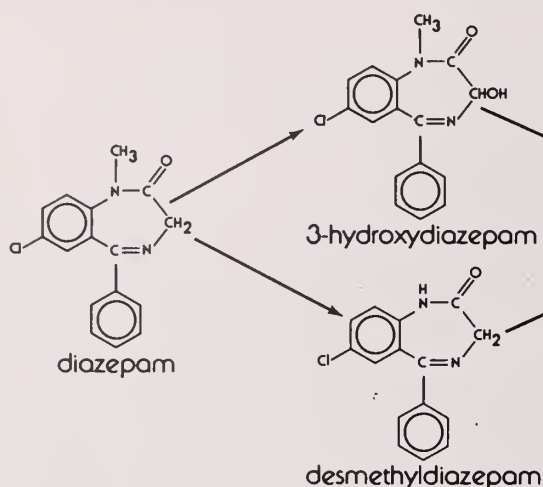
DISPLAY  
ELVES

FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

APR 21 1977

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET  
BOSTON, MASS. 02115

# A pharmacokinetic character all its own



**Valium (diazepam) is a benzodiazepine with a distinctive pharmacokinetic profile**

The pharmacokinetic profile of Valium is one of the characteristics that sets it apart from other benzodiazepines. Consider, in particular, the metabolic pathway of Valium. The three major metabolites of Valium exhibit significant pharmacologic activity—and so, of course, does the parent substance—diazepam itself. All combine to produce the characteristic clinical response seen with Valium. The response you have come to know, to want and to trust.

Pharmacokinetic studies also demonstrate that Valium has a pattern of absorption, distribution, metabolism and elimination that is reliable and consistent. And, although the pharmacokinetics of a drug cannot, at present, be specifically related to its clinical effects, it is clearly a factor that distinguishes one product from another by providing important insights into how each moves through the patient's body.

## Valium® (diazepam) <sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:**

Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma;

may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110





THE F  
L

**In reflux  
esophagitis, if  
she could sleep  
standing up...  
any antacid  
might do**

**Camalox<sup>®</sup>**

(magnesium and aluminum hydroxides with calcium carbonate)

**increases lower esophageal sphincter pressure  
to prevent acid reflux from occurring nocturnally  
when the patient is horizontal.<sup>1</sup>**

**Camalox...the high-potency, long-lasting  
antacid that stands up even when the patient  
lies down.**

1. Higgs, R.H., Smyth, R.D., and Castell, D.O., Gastric Alkalinization—  
Effect on Lower-Esophageal-Sphincter Pressure and Serum Gastrin,  
The New Engl. J. of Med., 291: 486-490, 1974.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034



**antifungal**

**antipruritic**

**antibacterial**

**anti-  
inflammator**



**TAXI**



# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform<sup>®</sup> Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

\*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform<sup>®</sup> Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

*This product is not for ophthalmic use.*  
In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm.

**Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

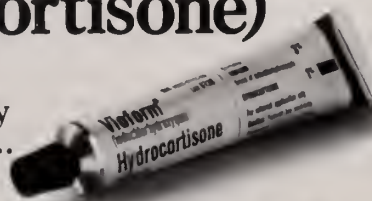
Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/6867 17

# Vioform<sup>®</sup> Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

Organo Oficial

Fundado en 1903

Volumen 69

Febrero 1977

Número 2

## JUNTA EDITORA

*José L. Cangiano, Presidente; Herman J. Flax; Norman I. Maldonado; F. Hernández Morales; Francisco Olazábal, Jr.; Nathan Rifkinson; Enrique O. Velez García; Antonio J. Grillo; Mario R. García Palmieri; Rafael Villavicencio Jiménez; E. A. Santiago Delpin; Ramón H. Bermúdez; Manuel Martínez Maldonado; José Juan Corcino; Jesús M. Vázquez; Osvaldo Ramírez Muxó.*

## SECRETARIO DE REDACCION

*Sr. Gregorio Díaz*

### Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

### Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

### Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

## CONTENIDO

Determinants of Human Water Contact Patterns in Urban Puerto Rico with Special Reference to Schistosomiasis .....	35
<i>Jan K. Lipes, MD and Robert A. Hiatt, MD</i>	
Recent Advances in the Diagnosis and in the Prevention of Rheumatic Fever .....	45
<i>Angelo Taranta, MD</i>	
Diarrea y Colitis Asociada a Antibióticos .....	55
<i>Carlos H. Ramírez Ronda, MD, FACP y Carlos León-Valiente, MD</i>	
Síndrome de Laurence-Moon-Biedl-Bardet. A Propósito de un Caso .....	60
<i>Adolfo Pérez Comas, MD, PhD</i>	
Evaluation of Cellular Mediated Immunity in a Normal Adult Population .....	64
<i>Francisco Robert, MD, José A. Lozada, MD and Francisco J. Muñiz, MD</i>	
Influenza — Treatment and Prevention .....	70
<i>Carlos F. León-Valiente, MD, Carlos H. Ramírez Ronda, MD, FACP and Ramón H. Bermúdez, MD</i>	
Editorial: Water Contact Patterns and Bilharziasis .....	74
<i>George V. Hillyer, PhD</i>	
Noticias .....	75

*PORTADA: Vista de fachada Santa Iglesia Catedral, Viejo San Juan (Cortesía del Dr. Rafael E. Ramírez)*



# DETERMINANTS OF HUMAN WATER CONTACT PATTERNS IN URBAN PUERTO RICO WITH SPECIAL REFERENCE TO SCHISTOSOMIASIS

Jan K. Lipes, M.D.  
Robert A. Hiatt, M.D.

**H**uman contact with bodies of fresh water is a key link in the chain of continuing contamination and infection by *Schistosoma mansoni*. Knowledge of human water contact behavior establishes a rational basis upon which programs for education about schistosomiasis and its control can be planned. To our knowledge, no studies have been directed toward the assessment of who engages in what type of water contact and why in modern urban Puerto Rico.

In the present study, we attempted to make this assessment by surveying three urban areas in metropolitan San Juan whose residents were of differing socioeconomic status. We used a questionnaire to collect data on personal and family characteristics and water contact behavior. By relating these characteristics to human water contact behavior, we hoped to determine which public health education and control measures would prove most useful.

We agree with Farooq, who stated: Studies of a sociological or anthropological nature, when designed to have relevance in the interruption of transmission, should concentrate upon learning enough about the habits, customs, beliefs and attitudes of the people so that those in charge of control programs can design acceptable alternatives to the dangerous habits leading to infection." (1)

The objectives of our study, then, were:

1. to investigate correlations between personal and family characteristics, such as age, sex, and socioeconomic status, and patterns of water contact.
2. to determine the principal reasons for contact with bodies of fresh water by persons residing in modern

urban Puerto Rico.

3. to determine the locations of water contact by the urban population.

4. to assess the degree of knowledge about schistosomiasis and its association with water contact.

5. to assess the demand for safe freshwater recreational sites.

## Materials and Methods

The questionnaire dealt with two broad categories—personal and family characteristics, and water contact behavior. Included in the former were questions about age, sex, occupation, education, current residence, and years of residence. Occupation and education were scored according to Green (2). An education score was determined for the female head of household because her education level was considered to be a better correlate of family health behavior than that of the male head (2). A two-factor socioeconomic status (SES) index was calculated as the sum of weighted scores for occupation and education as recommended by Green (2). For some analyses, occupation was divided into groups of similar vocations to which we assigned arbitrary numbers from 0 to 8 according to the decreasing prestige of the occupation. All members of the household were assigned the same educational and occupational score and the same SES index. Although income adds a valuable third factor to the determination of SES, it was not considered feasible to obtain this information.

The second part of the questionnaire, water contact patterns, dealt with the presence and nature of water contact during the year prior to the interview (January to December 1975). If there was no water contact, we inquired why. If there was water contact, we asked how many times, the principal reason for the water contact, the months during which it occurred, and who accompanied the subject. All subjects were asked about their knowledge of schistosomiasis and their aspirations for use of safe freshwater recreational sites. Knowledge of the parasite was assessed by asking what bilharzia is and scoring the elements of the response with one point for each correct item mentioned. We considered four components of the transmission cycle to be important: 1) *S. mansoni* is a parasite; 2) the snail is an essential vector

From the San Juan Laboratories, Bureau of Laboratories, Center for Disease Control, Public Health Service, U. S. Department of Health, Education, and Welfare, GPO Box 4532, San Juan, Puerto Rico 00936.

Send reprint requests to this address.

TABLE I  
URBANIZATION CHARACTERISTICS

Characteristics	U R B A N I Z A T I O N S		
	College Park	Santiago Iglesias	Monacillo
Population *	1,916	4,535	1,421
No. of houses **	556	900	318
Mean no. of houses per block **	25.3	37.5	28.9
Mean no. of persons per household *	3.44	5.04	4.47
Approximate mean value of houses *	\$35,000	\$14,000	\$3,800

\* U. S. Census, 1970

\*\* Estimates from surveys and area maps

in its transmission; 3) humans contaminate water with feces; and 4) water contact is essential for humans to become infected. If none of these were mentioned, the score was 0; if one was mentioned, the score was 1; if two were mentioned, the score was 2, and so on.

We interviewed every person in the household individually, except in those cases where a particular member of the family was not present on several revisits. If the informant was reliable (usually a parent or older sibling), his or her answers to the questions about the missing person were accepted. If no one was home, we revisited the dwelling at a later time. If, after five visits, we found no one home, we designated the dwelling as a "no-show".

The questionnaire was administered to all individuals by the same trained interviewer. Children under 10 years of age were considered unreliable sources of information, and their responses were confirmed for validity with the parent or guardian. All those over 10 years of age were considered to be capable of giving valid responses.

From work in progress (3), information was obtained on some basic population characteristics of three communities in metropolitan San Juan. The three chosen for study included two relatively modern housing developments, College Park and Santiago Iglesias, and one low-cost housing area, Monacillo, all of which are adjacent to one another. For convenience, all three communities are referred to as "urbanizations" in this paper. Detailed maps had previously been constructed and preliminary information was available from census data and area surveys (Table I).

From an estimated total population of 7,872 in the three urbanizations, we wished to sample approximately 10 percent. Single family dwellings were listed and assigned a number. On the basis of an average household size of 4.1 persons, a random sample of 213 dwellings was chosen from the three areas for interviews. Households were chosen in proportion to the total number in each urbanization.

## Results

Information was obtained from 207 (97 percent) of the 213 households in the sample, thereby generating data on 772 household members. Three hundred and fourteen (41 percent) of the interviews were conducted with the respondent present, and 458 (59 percent) were conducted with an informant giving information about another family member. Sex and age of individuals in the sample are shown in Table II.

The mean size of families in each urbanization in our sample was more uniform than the 1970 census estimates (Table III). However, the impression of differentials in SES between urbanizations, originally based on observation and the data presented in Table I, was borne out by the analysis of occupational and educational scores in this study. The mean occupational rank and level of education were highest in College Park and lowest in Monacillo. The mean SES index, calculated on the basis of these two factors, also increased in a clear gradient from Monacillo to College Park.

The distribution of SES indices by household (Figure 1) has three major modes. Three groups were chosen on the basis of divisions at the two major troughs in this distribution: Group I, "low" SES (indices 28-46); Group II, "middle" SES (47-62); and Group III, "high" SES (63-80). Although there was considerable overlap, these groups displayed the range of SES indices exhibited by most of the households in each urbanization.

TABLE II  
SEX AND AGE OF INDIVIDUALS IN POPULATION SAMPLE FROM  
THREE URBANIZATIONS IN METROPOLITAN SAN JUAN, PUERTO RICO

Age (years)	Males		Females	
	No.	Percent	No.	Percent
0-9	62	16	41	11
10-19	91	23	71	19
20-29	54	14	65	17
30-39	35	9	46	12
40-49	58	15	73	19
50-59	39	10	43	11
60-69	24	6	29	8
≥ 70	26	7	15	4
TOTAL	389	100	383	100

TABLE III  
CHARACTERISTICS OF POPULATION SAMPLE  
FROM THREE URBANIZATIONS

Characteristics	U R B A N I Z A T I O N S		
	College Park	Santiago Iglesias	Monacillo
No. of people in sample	246	367	159
No. of households	67	98	42
Mean no. persons per household	3.67	3.74	3.79
Mean occupational score *	4.3	3.0	1.3
Mean educational score **	4.1	2.5	1.6
Mean socioeconomic status ***	67.0	52.5	43.2

\* Principal household provider

\*\* Female head of household

\*\*\* See Methods

One hundred and seventy-nine (23 percent) of 772 individuals interviewed, or at least one person in 71 (34 percent) of 207 households, admitted to water contact in the past year (Table IV). Of those individuals who said they had had water contact, 74 (41 percent) had it only once, 127 (71 percent) and contact fewer than five times, and only 7 (4 percent) had contact more than 50 times during the year. More males admitted to water contact than females (28 percent vs. 19 percent), but there was no sex difference with regard to the number of times an individual had water contact. With regard to age, between 29 and 33 percent of the persons in the

0- to 4-year, 5- to 19-year, and 20- to 29-year age groups had water contact, as compared with only 16 percent of those over age 30.

Eighteen (28 percent) of the 5- to 10-year olds reporting water contact admitted to more than 10 episodes during the year.

The proportion of people admitting to water contact decreased as the affluence of the urbanization increased. Thirty-six percent of Monacillo residents, but only 15 percent of College Park residents, had had contact with bodies of fresh water in the previous year. The differences between these proportions was significant ( $X^2$ , goodness of fit,  $p < .001$ ). However,



TABLE IV  
NUMBER OF INDIVIDUALS WITH WATER CONTACT AND  
THE FREQUENCY OF CONTACT BY AGE

Age (Years)	No. Interviewed	No. of Water Contacts in Last Year					Total
		1	2-4	5-9	10-49	50 +	
0-4	42	7 (58) *	1 (8)	3 (25)	0 (0)	1 (8)	12
5-19	223	23 (35)	18 (28)	5 (8)	18 (28)	1 (2)	65
20-29	119	14 (36)	18 (46)	2 (5)	4 (10)	1 (3)	39
30 +	388	30 (48)	16 (25)	4 (6)	9 (14)	4 (6)	63
TOTAL	772	74 (41)	53 (30)	14 (8)	31 (17)	7 (4)	179

\* Total no. (Percent) of water contacts in that age group.

TABLE V  
NUMBER OF INDIVIDUALS IN CATEGORIES DEFINED BY  
URBANIZATION AND SOCIOECONOMIC STATUS AND THE PERCENT OF  
THESE INDIVIDUALS WITH WATER CONTACT DURING PREVIOUS YEAR

	U R B A N I Z A T I O N			Total number of individuals in SES group
	Monacillo	Santiago Iglesias	College Park	
Group I "Low"	105 (37) *	119 (15)	4 (0)	228 (25)
Group II "Middle"	54 (35)	190 (26)	53 (4)	297 (24)
Group III "High"	0 (0)	58 (29)	189 (19)	247 (21)
Total number of individuals in urbanization	159 (36)	367 (23)	246 (15)	772 (23)

\* Number of individuals interviewed (percent) with history of water contact during previous year.

the proportions of people with water contact in the three SES groups were not significantly different (Table V). The discrepancy between urbanization and SES with respect to history of water contact seems superficially inconsistent given the direct association between urbanization and SES; however, it is clarified by looking at the occurrence of water contact by SES within each urbanization. The only urbanization with good representation in all SES groups was Santiago Iglesias, where, in fact, more people in the higher SES groups reported water contact. These differences, however, were not significant (by  $X^2$  goodness of fit test). In all urbanizations there is more homogeneity in these proportions than within SES groups.

The months in which water contact was most frequent (61 percent of all contact) were June, July, and August. These months were the most popular irrespective of SES or urbanization. Seventeen percent of those surveyed admitted to water contact year round, but they were primarily those with low SES and residents of Monacillo.

In this study the family was the most important social unit associated with water contact. Of all individuals who had had water contact, 126 (70 percent) had done so with their families, 36 (20 percent) had done so with friends, and 17 (10 percent) alone.

The 31 water contact sites were located over the

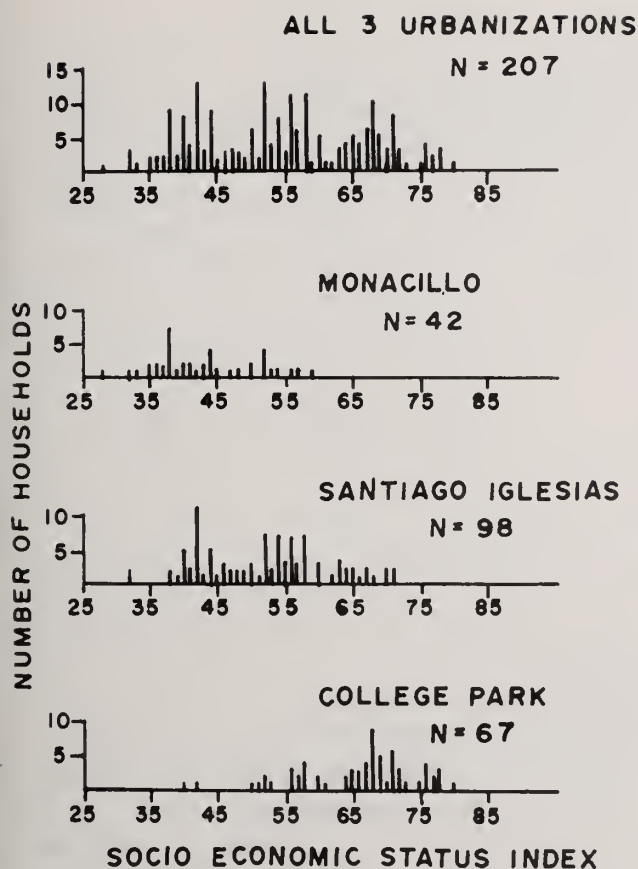


Fig. 1: Distribution of household socioeconomic scores by urbanization, metropolitan San Juan, Puerto Rico.

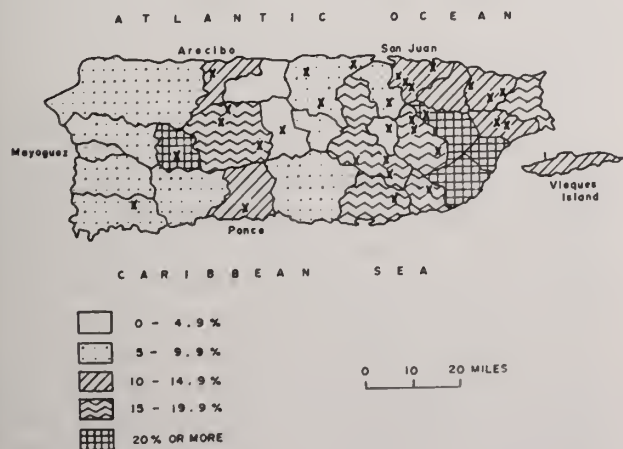


Fig. 2: Location of water contact sites of residents of metropolitan San Juan on map of prevalence rates for 1969 Schistosomiasis Mansonii skin test survey by watershed area.

entire island, although most sites reported (74 percent) were in the eastern half. These 31 locations are plotted on a map which also shows the results of an islandwide skin test survey in 1969 (4) (Figure 2). Table VI demonstrates that most of the people who admitted having water contact had the contact in watershed areas with relatively high skin test positivity rates. The areas used by the most people were: 49 persons (27 percent) - El Verde in the El Yunque Forest area; 21 persons (12 percent) - Doña Ana, the stream in Monacillo; 12 persons (7 percent) - Lago Carraízo in Trujillo Alto; 9 (5 percent) - Río del Yunque in Luquillo; 8 (4 percent) - Dos Bocas Lake in Utuado; 7 (4 percent) - Río Unibon in Morovis; and 6 each (3 percent) - Jayuya River, Río La Plata in Dorado, and streams in Guaynabo and Vega Baja.

All 21 persons who admitted contact with the stream in Monacillo were from that community. Thirteen of the 21 (62 percent) were in the 5- to 19-year age group, and 9 of these had frequent contact ( $\geq 10$  times during the year), primarily while fishing.

The principal reasons for water contact were swimming and fishing (Table VII). Forty seven percent of all individuals with contact reported swimming as their principal activity, and 20 percent reported fishing. Other activities included "splashing to cool off" (14 percent), "playing" (12 percent), "washing hands and feet" (10 percent), and "washing objects" (6 percent). More females swam than males (51 percent vs. 45 percent), and more males fished than females (25 percent vs. 11 percent). With increasing SES and increasingly affluent urbanization, the frequency of swimming increased and the frequency of fishing decreased. In Monacillo, the most frequent water contact (31 percent) was fishing, whereas in College Park and Santiago Iglesias, swimming was most common (57 percent and 59 percent of all contact, respectively). After the age of 4 years, no relationship was seen between age and the type of water contact.

Although the number of people who had heard of the term "bilharzia" was high (95 percent) for all reliable individuals over 10 years of age irrespective of SES or urbanization, there were differences in the degree of knowledge. The mean knowledge score increased with increasing SES: Group I, 1.79; Group II, 2.14; Group III, 2.46. Also, if the small number of individuals (7) who knew nothing about schistosomiasis is not considered, it was noted that there was a tendency to have less water contact the more knowledge the individuals possessed (Table VIII).

**TABLE VI**  
**LOCATION OF WATER CONTACT SITES IN RELATION TO**  
**WATERSHED SKIN TEST PREVALENCE BASED ON 1969 SKIN TEST SURVEY**

Watershed prevalence	No. of water contact sites	Persons involved in water contact	
		No.	Percent
0-4.9 percent	2	4	2
5-9.9 percent	5	27	15
10-14.9 percent	11	94	53
15-19.9 percent	11	49	27
20 percent or more	2	5	3
TOTAL	31	179	

**TABLE VII**  
**FREQUENCY OF SWIMMING AND FISHING AS PRINCIPAL**  
**REASONS FOR WATER CONTACT IN 170 INDIVIDUALS**

	U R B A N I Z A T I O N			SOCIOECONOMIC STATUS		
	Monacillo	Santiago Iglesias	College Park	Group I "Low"	Group II "Middle"	Group III "High"
Swimming	15 (26) *	48 (57)	22 (59)	21 (37)	34 (49)	30 (58)
Fishing	18 (31)	15 (18)	2 (5)	13 (23)	18 (26)	4 (8)
Total No. with water contact	58	84	37	57	70	52

\* Number (percent) of total water contact in urbanization or SES group.

With regard to the demand for bilharzia-free recreational areas, approximately 65 percent of all heads of households said they would use fresh water for recreation if bilharzia-free areas were available. This figure was independent of SES.

### Discussion

It is apparent from this study that many persons living in an urban environment in Puerto Rico continue to seek out and have contact with freshwater streams

and lakes. As long as schistosomiasis is endemic in Puerto Rico, these activities increase the risk of transmission. The principal reason for water contact appears to be recreation, especially if the locations of contact are distant from the urban environment.

In contrast to patterns seen in less developed nations, we found that males had more episodes of water contact than females. Husting (5), observing the rural Bantu in Rhodesia, and Farooq and Mallah, observing various segments of the population in Egypt (6), found that females had more contact than males. The dramatic increase in the number of homes with piped water (7) may help account for this sex difference in water contact. Females in less developed nations still use



TABLE VIII  
DEGREE OF KNOWLEDGE OF BILHARZIA IN 632 INDIVIDUALS  
OVER 10 YEARS OF AGE IN RELATION TO REPORTED  
WATER CONTACT IN PREVIOUS YEAR

Knowledge Score	Percent with water contact	Total Interviewed
0	14	7
1	32	129
2	21	318
3	25	125
4	17	53
TOTAL	23	632

natural water bodies to perform numerous traditional household chores, such as washing clothes and cooking utensils, whereas, in Puerto Rico, most females use water piped into the home.

Sixty-five percent of water contact was by persons under 30 years of age, and half of those who admitted to contact more than 10 times during the year were 5 to 19 years old. This observation is consistent with the finding of peak prevalence of infection in young adults in Puerto Rico. Most persons had water contact less than four times in the year, which indicates that, in Puerto Rico, water contact is not an integral part of the daily activities of housework or occupation.

June through August was the period of greatest water contact for all persons, irrespective of SES. An increased risk of infection exists at this season because higher water temperatures and more sunlight favor the proliferation of the intermediate host snail and the transmission of *S. mansoni*. In Monacillo, the urbanization with the lowest SES, a large number of persons had year-round water contact. Several factors may be responsible. One is that a stream (Doña Ana) is situated along the periphery of Monacillo, and 37 percent of the water contact from the community was in this stream. The ready availability of this stream may be a factor in its frequent use. However, proximity of a stream is not unique to Monacillo. Streams also meander through various parts of Santiago Iglesias and College Park, but were not used by their residents. Although fencing and channelization

of all of these streams exist at various points, these improvements are by no means uniform or complete, and they cannot be considered a deterrent to water contact. It is likely that Monacillo residents turn to Doña Ana for recreation because of lack of transportation, whereas, in the other urbanizations, the ready availability of automobiles provides easy access to freshwater facilities located great distances away.

A lack of play facilities for youngsters, more ample in the urbanizations of higher SES, may encourage children and young adults to turn to the Monacillo stream for recreation. Thirteen of 21 with contact in Doña Ana were children between 5 and 19 years of age, and most of these children had frequent contact. The fact that *Biomphalaria glabrata* infected with *S. mansoni* were recovered from this stream in 1971 (8) adds a special note of concern to this observation.

For all persons studied, swimming was the recreational activity engaged in most frequently. This activity, which often by its very nature involves whole body contact for significant periods of time, offers optimal conditions for penetration of skin by schistosome cercariae. Fishing activity was close to swimming in frequency, and, in Puerto Rico, this activity often takes the form of whole body immersion in search of small freshwater shrimp rather than standing on shore and using a rod and reel. The fact that fishing was far more popular in the lower SES group than in the higher may be due to the fact that this is an inexpensive,

readily available pastime which also provides food. It is not surprising that males fish more than females; the traditional "masculine" nature of the activity may be derived from its original significance as an important method of obtaining food for the family. All other types of water contact, including washing objects, bathing, fording streams, collecting water, etc., were reported in low frequency in this study.

These results are in contrast to other areas of the world where customs and behavior are different. Thus, Husting (5) in Rhodesia found that the most common activities were washing dishes, collecting water, bathing, and swimming. Farooq and Mallah (6) in Egypt noted that the most frequent water contact activities were washing utensils, bathing, playing, and ritual washing. In Puerto Rico, Jobin and Ruiz-Tibén (9) performed field observations of water contact in Llanos Adentro, a rural burrough of Aibonito in 1966, and found that the greatest exposure to fresh water occurred during play activity by school children. Thus, the nature of water contact in Puerto Rico, which is primarily recreational and lacks an occupational and domestic component, differs markedly from that of these less developed areas.

It is striking that the urban population of San Juan engages in such geographically widespread water contact (Figure 6). The willingness of people to travel to distant parts of the island illustrates the demand for freshwater recreation. Most of the water contact occurred in the eastern part of the island, where schistosomiasis prevalence is highest (4). This is partially related to the fact that the population lives in eastern Puerto Rico, but may also be due to the attraction of the many freshwater streams in the area. It is of much concern that so many individuals in our urban sample used bodies of fresh water in areas where the prevalence of schistosomiasis was high. This fact demands that greater efforts be made to study the water contact patterns of individuals islandwide, with the goal of eliminating the risks of infection. Indeed, the demand for safe, freshwater facilities, as gauged directly by our questionnaire, was overwhelmingly affirmative and unaffected by SES.

Surprisingly, we found that individual or family SES was not correlated with the occurrence of water contact. This observation is, however, compatible with the findings of Weller and Dammin in 1945, who found similar stool prevalence rates of *S. mansoni* in all occupational groups in their survey of World War II recruits in Puerto Rico (10). On the other hand,

there was a decrease in the proportion of individuals admitting to water contact associated with increasing affluence of the urbanization (Table V). This apparent inconsistency was due to the tendency of water contact behavior to be more homogeneous within urbanization than within SES group. This suggests that there is some characteristic of residents of the same urbanization that may determine water contact behavior, but which is not measured by our SES index.

The proportion of people admitting to water contact decreased as the level of knowledge of bilharzia increased (Table VIII). This was true even though our crude four-factor index measured only the biologic aspects of the cycle and not other important characteristics of the disease and its transmission.

We believe that the results of this study can be useful in two ways. First, the frequency of water contact in Doña Ana in Monacillo, especially by younger individuals, has been shown to require attention. Despite channelization of a large portion of this stream, vegetation has become reestablished and can provide an ideal habitat for *B. glabrata* \*. Transmission can occur in urban streams such as this, and at least two outbreaks of acute schistosomiasis were seen in 1975 from such sources (R. A. Hiatt, unpublished). There is a definite need to upgrade the maintenance of these urban streams and to focus snail surveillance activities in suspected trouble areas.

Second, in more general terms, this study indicates that relatively simple, community-based questionnaire surveys are a valuable source of behavioral information with regard to schistosomiasis transmission in Puerto Rico. Standardized questionnaire studies in representative island communities could be a powerful tool in identifying the recreational sites potentially important in transmission. They are a logical next step after islandwide skin test prevalence surveys which pinpoint the particular watersheds where transmission occurs. In addition, information from such questionnaires can provide data on who is at risk from water contact, the time of year that the risk occurs, and the reasons for it. This information is necessary to properly direct efforts in health education as well as snail surveillance,

\* The upper reaches of Doña Ana Creek have been known to be infested with *B. glabrata* for many years. A snail check during October 1976 confirmed the presence of *B. glabrata* a few meters above the beginning of the concrete channel.

mollusciciding activities, and stool surveys. It is almost impossible for health authorities to keep track of all potential water contact sites and snail habitats in Puerto Rico. Questionnaire surveys would allow them to focus on sites where water contact is most likely to occur.

Observational studies at the sites identified by questionnaire surveys can provide additional information on the "who" and "when" of water contact behavior. Such studies have the obvious advantage of documenting activity on-the-spot without the problems of weak or inaccurate recall. In addition, individuals can be interviewed at the site of contact to obtain data on residence and frequency of visits to freshwater recreational sites.

In summary, the present study analyzed the human behavioral component of exposure in the transmission of *S. mansoni* in Puerto Rico. We found that recreational contact with fresh water was a common, seasonal occurrence among a randomly selected group of urban San Juan residents. Many sites are chosen for such activity, and they are widely dispersed throughout the island—a good number are in the areas most endemic for schistosomiasis. Puerto Rican streams and lakes are used for recreational purposes by all socioeconomic groups, but slightly less frequently as the level of knowledge of the transmission cycle increases. Further investigations are needed to assess the presence of *S. mansoni* infection in these individuals and, therefore, the risk of schistosomiasis associated with the water contact activity described.

### Summary

A standardized questionnaire was used in a survey made in three urban San Juan neighborhoods to determine the frequency and characteristics of water contact practices as potential risk factors in the transmission of schistosomiasis. Twenty-three percent of the 772 individuals surveyed admitted they had come in contact with freshwater streams in Puerto Rico in the previous year. Recreational swimming and fishing accounted for almost 70 percent of water contact. Families from all socioeconomic and age groups were involved, although children in the 5- to 19-year age group were more likely to have frequent contact. Freshwater locations were widely distributed throughout the island, but most of the persons involved went to watershed areas in the eastern part of the island where prevalence of schisto-

somiasis is highest. There was a tendency for those with better knowledge of "bilharzia" (schistosomiasis) to have less water contact. Studies such as the one described would provide valuable information for planning islandwide health education and control programs.

### Resumen

Utilizando un cuestionario estándar se estudiaron tres áreas urbanas de San Juan con el propósito de determinar la frecuencia y otras características del contacto humano con cuerpos de agua como un factor de riesgo potencial en la transmisión de la esquistosomiasis. De las 772 personas incluidas en el estudio, 23 por ciento admitieron haber estado en contacto con cuerpos de agua dulce durante el año anterior. La natación y la pesca recreativa fueron la razón para el contacto en cerca de un 70 por ciento de los casos. Contacto con agua dulce ocurrió en familias de todos los niveles socioeconómicos y en todas las edades pero fueron los entrevistados entre los 5 y los 19 años de edad los más aptos a tener contacto frecuente. La distribución geográfica de los cuerpos de agua utilizados abarcó toda la Isla pero se indicó una preferencia por el uso de cuencas hidrográficas en la región este del país en donde prevalece la esquistosomiasis. Se observó una tendencia a evitar contacto con focos potenciales de infección entre las personas con un mayor conocimiento con respecto a la "bilharzia" (esquistosomiasis). Estudios similares a éste podrían proveer información de mucho valor en la planificación de programas de educación y de control de la enfermedad para toda la Isla.

### Acknowledgments

We would like to thank Aníbal Carrión for his tireless assistance during our survey and Ernesto Ruiz-Tibén for his advice on all aspects of this study. Deep appreciation is expressed to the Department of Community Medicine of the Albert Einstein College of Medicine, New York, under whose auspices the Manealoff Fellowship was granted so that this project could be undertaken.

### References

1. Farooq, M.: Pre-control investigations in bilharziasis.



- J Trop Med Hyg 72: 14-17, 1969.
2. Green, L.: Manual for scoring socioeconomic status for research on health behaviour. Public Health Reports 85: 815-827, 1970.
  3. Ruiz-Tibén, E.: Determinants of *Aedes aegypti* abundance distribution in Puerto Rico. Doctoral thesis protocol, 1975.
  4. Ruiz-Tibén, E., Cox, P. M. Jr., Clark, W. D., and Greenberg, E. R.: The 1969 schistosomiasis skin test survey in Puerto Rico. Bol Asoc Médica de P. Rico 65 (7): 170-173, 1973.
  5. Husting, E.: Sociological patterns and their influence on the transmission of bilharzia. Cent African J Med 16 (Suppl): 5-10, 1965.
  6. Farooq, M. and Mallah, M. B.: The behavioural pattern of social and religious water contact activities in the Egypt-49 Bilharziasis Project Area. Bull WHO 35: 377-387, 1966.
  7. Cline, B.: Control of schistosomiasis in Puerto Rico. Pages 97-99 in M. J. Miller, ed., *Proceedings of a Symposium on Schistosomiasis Control*. Tulane University, New Orleans, 1972.
  8. Ruiz-Tibén, E.: Personal communication. San Juan Laboratories, Center for Disease Control, San Juan, Puerto Rico, 1971.
  9. Jobin, W. and Ruiz-Tibén, E.: Bilharzia and patterns of human contact with water in Puerto Rico. Bol. Asoc. Médica de P. Rico, 60: 279-284, 1968.
  10. Weller, T. H. and Dammin, G. J.: The incidence and distribution of *Schistosoma mansoni* and other helminths in Puerto Rico. P Rico J Public Health and Trop Med 21: 125-147, 1945.

# RECENT ADVANCES IN THE DIAGNOSIS AND IN THE PREVENTION OF RHEUMATIC FEVER

Angelo Taranta, MD

Having been invited to write on recent advances in the diagnosis and prevention of rheumatic fever, I am tempted to start, like a character in "Alice in Wonderland" did once: "I will tell you everything I know: there is little to relate". Since the recent advances have been few and unspectacular, I will stretch a bit the meaning of the word "recent" to cover all that I want to discuss. After all, as another Lewis Carrol (1) character remarked on another occasion, "A word means exactly what I want it to mean, neither more nor less".

## Part One: Diagnosis

Contrary to all hopes, contrary also to some misconceptions, we still don't have a test specific for rheumatic fever. This does not mean that laboratory tests are of no use in this diagnosis, just that they serve a subsidiary role (1), and that rheumatic fever remains a clinical diagnosis, based on the revised Jones criteria (2). Figure 1 shows the list of major and minor manifestations of rheumatic fever. The only substantive change in this latest revision of the criteria is that evidence of a streptococcal infection has been removed from the minor manifestations where it clearly didn't belong and put at the bottom of the list as it becomes to a foundation. Regarding the various major manifestations, subcutaneous nodules are very rare these days (Figure 2), and so is erythema marginatum (Figure 3) — so rare, in fact, that many young physicians have never seen them. Chorea (Figure 4) with its characteristic grimaces and involuntary movements of the limbs is more common, but still accounts only for a small minority of the rheumatic fever

patients. The bulk of them have arthritis and carditis, single or in combination.

One of the most common diagnostic errors used to be the overdiagnosis of rheumatic fever. Before the Jones criteria became popular, every child with a low grade fever and a pale skin was considered rheumatic until proved otherwise; if there was an ache in a limb so much the better. We see this much less now, but still too often: in our own survey of children admitted to a convalescent home 7 percent were overdiagnosed in this way — despite the fact that these patients had already been filtered through a referring hospital (3). When they have not been so filtered the percentage of overdiagnosis is larger; in some of the large-scale rheumatic fever prophylaxis clinics operated by private, local, and state agencies, it has been estimated that the original diagnosis of rheumatic fever is dubious or incorrect in 10 to 30 percent of the patients (Figure 5). Overdiagnosis is often due to arthralgia mistaken for arthritis; to daytime tachycardia, often emotional in origin and absent during sleep, or prolongation of the P-R interval being considered evidence of carditis; or to a physiologic apical systolic murmur being misinterpreted as organic because its loudness is increased by fever. This misdiagnosis of minor, self-limited illnesses as rheumatic fever is a serious matter, since it fosters cardiac neurosis, invalidism, and cardiac non-disease.

The other major kind of diagnostic error occurs when a serious organic disease is present, is not properly diagnosed, and is misinterpreted as rheumatic fever (Fig. 6). Children with juvenile rheumatoid arthritis often start off this way, but lupus, osteomyelitis, congenital heart disease accompanied by fever, congestive failure, or both may cause similar puzzlements and errors. They all can be properly diagnosed by "thinking of them" and by appropriate tests. In the case of juvenile rheumatoid arthritis or lupus little is lost by this error of diagnosis, since all of these diseases are treated with anti-inflammatory drugs. But in the case of an infection, such as osteomyelitis or bacterial

*From the Departments of Medicine, Cabrini Health Care Center and New York University School of Medicine, New York, N. Y.*

*Address reprint requests to Angelo Taranta, MD, Cabrini Health Care Center, 227 East 19th Street, New York, N. Y., 10003.*

## JONES CRITERIA (REVISED) FOR GUIDANCE IN THE DIAGNOSIS OF RHEUMATIC FEVER

MAJOR MANIFESTATIONS		MINOR MANIFESTATIONS	
Carditis		Clinical	Laboratory
Polyarthrititis		Previous rheumatic fever or rheumatic heart disease	Acute phase reactions: Erythrocyte sedimentation rate, C-reactive protein, leuko- cytosis
Chorea			
Erythema Marginatum		Arthralgia	
Subcutaneous Nodules		Fever	Prolonged P-R interval

SUPPORTING EVIDENCE OF STREPTOCOCCAL INFECTION	
Increased titer of streptococcal antibodies, such as ASO (antistreptolysin O)	
Positive throat culture for group A streptococcus	
Recent scarlet fever	

Fig. 1: Major and minor manifestations of rheumatic fever,  
and supporting evidence of streptococcal infection.



Fig. 2: Subcutaneous nodules on the elbow, the knuckles and the temporal region of children with rheumatic fever. (Courtesy of Dr. Eugenie Doyle.)

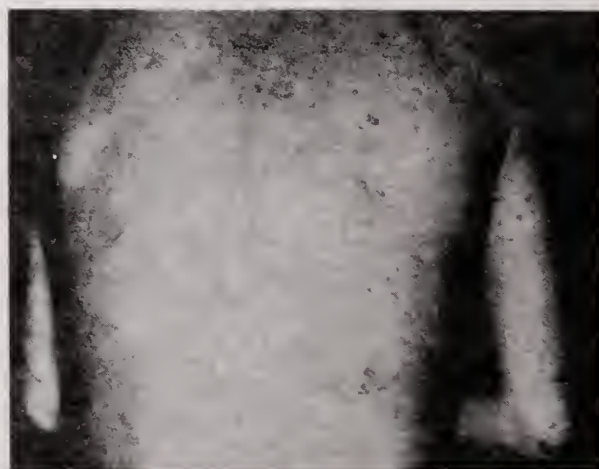


Fig. 3: Erythema marginatum, the characteristic, evanescent rash of rheumatic fever.

endocarditis, the administration of anti-inflammatory drugs may suppress the symptoms and allow the infection to progress. Of particular interest is the case of bacterial endocarditis, because of its relative frequency and its severe nature. Error is easy and common because bacterial endocarditis shares with rheumatic fe-

ver a number of manifestations, including arthralgia and arthritis. Figure 7 shows that the pattern of joint involvement in bacterial endocarditis is the same as in rheumatic fever; relatively large joints with some preference for the lower limbs. The arthritis of bacterial endocarditis may be fixed in one joint (Figure 8); but





Fig. 4: Sydenham's chorea or chorea minor, evidenced by involuntary grimacing. (Taranta in Hollander & McCarty, Arthritis, courtesy of Lea & Febiger).

## COMMON ERRORS IN THE DIAGNOSIS OF RHEUMATIC FEVER

1. Failure to use the Jones criteria or incorrect application of them:
  - a. Arthralgia mistaken for arthritis.
  - b. Emotional tachycardia or prolongation of the P-R interval mistaken for definite evidence of carditis.
  - c. A physiologic systolic murmur made louder by fever — and mistaken for a pathologic murmur.

Common consequence: A minor illness is misdiagnosed as rheumatic fever.

Fig. 5: Errors in the diagnosis of rheumatic fever.

may also migrate from joint to joint like the classical migratory arthritis of rheumatic fever.

The demonstration of a recent or still present group A streptococcal infection will strengthen the case for rheumatic fever. This demonstration can be accomplished at times by throat culture (Figure 9); which may reveal lingering beta-hemolytic streptococci (Figure 10). More often, however, the streptococci have disappeared from the throat by the time rheumatic fever appears so that the only trace left is in the blood, (Figure 11). Antibody determinations will reveal the

## COMMON ERRORS IN THE DIAGNOSIS OF RHEUMATIC FEVER

### 2. Uncritical reliance on the Jones criteria:

- a. Many patients may "fulfill" the Jones criteria, yet have other diseases (rheumatoid arthritis, bacterial endocarditis, congenital heart disease with congestive failure precipitated by an infection, osteomyelitis, lupus erythematosus, etc.). Evidence of a preceding streptococcal infection will reduce, but not eliminate, the possibility of these errors.

Fig. 6: Other errors in the diagnosis of rheumatic fever.

## SITE OF JOINT INVOLVEMENT WITH BACTERIAL ENDOCARDITIS

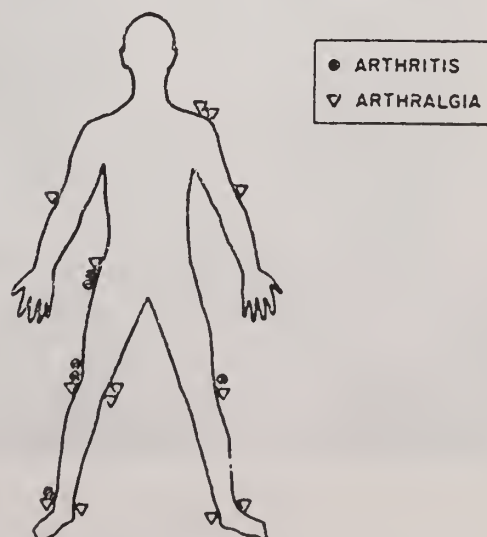


Fig. 7: Pattern of localization of arthritis and arthralgia in patients with bacterial endocarditis.

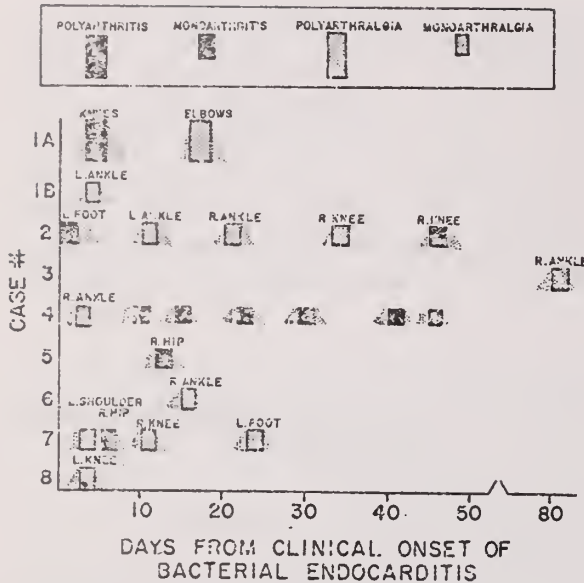


Fig. 8: Sequence of joint involvement in patients with bacterial endocarditis.



Fig. 9: Taking a throat culture to detect group A beta hemolytic streptococci.

previous presence of a streptococcal infection (Figure 12), and if one adds to the ASO one or two other streptococcal antibodies the percentage of positivity approaches 100 percent in patients with confirmed rheumatic fever (4). An exception must be noted in the case of chorea, in which streptococcal antibodies may be low (Figure 13), possibly due to a strangely long latent period that has been documented in these children between the streptococcal infection and the onset of chorea — so long that it allows the streptococcal antibody titers, elevated initially, to fall back to pre-infection levels (5).

In recent years two other streptococcal antibody tests have been developed, the anti DPNase (6) and anti DNA-se B (7) which are somewhat simpler to perform than the antihyaluronidase and antistreptokinase tests and are currently favored as "second tests" (with the ASO remaining the test usually done first). In addition, the anti DNA-se B has two peculiarities that may make it useful in special cases; it is often elevated in children with streptococcal pyoderma, an infection which often fails to stimulate a rise of ASO; and it remains elevated for a longer time than the other streptococcal antibodies — therefore it may be useful in the study of children who present with chorea or who for some other reason come to medical attention long after the eliciting streptococcal infection.

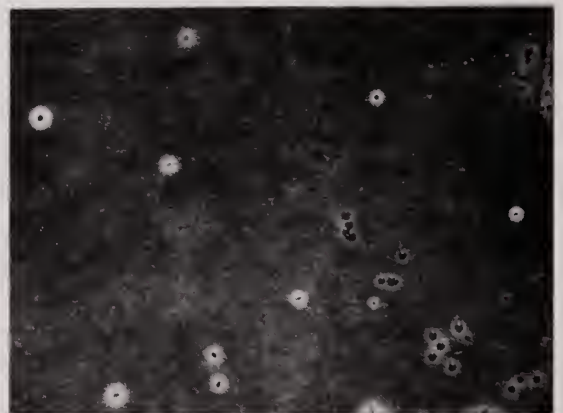


Fig. 10: Group A beta hemolytic streptococci growing on the surface (narrow clear halo) and under the surface (wide clear halo) of a blood agar plate. (Taranta & Moody, courtesy of *Pediatr. Clin. North Am.*)



Fig. 11: Taking a blood sample for streptococcal antibody determinations.

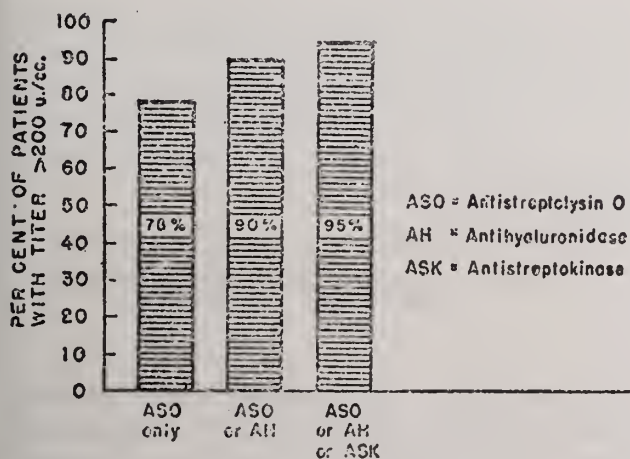


Fig. 12: Percentage of positive streptococcal antibody titers in patients examined within two months from the onset of rheumatic fever. (Stollerman et al., courtesy of Am. J. Med).

All these antibody determinations are based on the inhibition of the specific toxic or enzymatic activity of a given streptococcal product — streptolysin O, streptokinase, etc. Very recently, another test has been developed which is based on another principle, namely

the agglutination of red cells, coated with streptococcal extracellular products, by antibodies against these extracellular products (8) (Figure 14). This figure shows how a negative test looks, on the left, compared to a positive test, on the right. The preparations used for sensitization of the red cells is a mixture of antigens, but the results indicated on the horizontal axis correlate quite well with those of the ASO test indicated on the vertical axis (Figure 15). If we use arbitrary cut-off points, such as 166 u. for the ASO and 1:100 for the streptozyme test, as the upper limits of normal, then we have 6 percent false-negative and 28 percent false positive — with respect to the ASO. There are indications that a substantial percentage of these sera contained other streptococcal antibodies, and did not represent therefore false-positive results. The streptozyme test, as this new agglutination test has been called, gives a result in two minutes and can be performed on a drop of blood. It was originally introduced as a screening test but may well end up by competing with the ASO test. According to several investigators, this agglutination test may detect an antibody response in patients with streptococcal pyoderma who have no ASO rise. Other antibodies of potential diagnostic usefulness

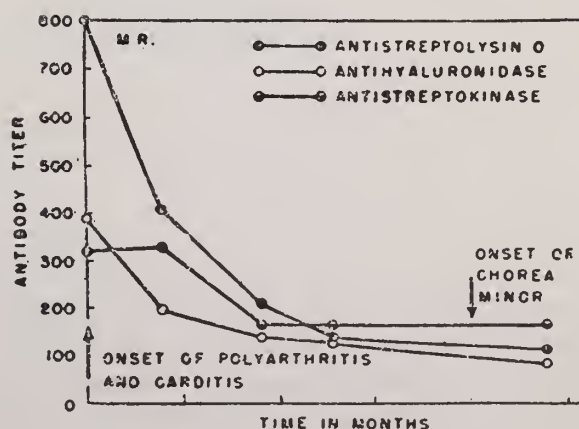


Fig. 13: Late development of chorea in a patient with previous polyarthritis and carditis. The steady fall of the three streptococcal antibodies excludes intercurrent streptococcal infections. (Taranta & Stollerman, courtesy of Am. J. Med.)





Fig. 14: Negative and positive streptococcal passive hemagglutination test (streptozyme). (Janeff et al., courtesy of Lab. Med.)

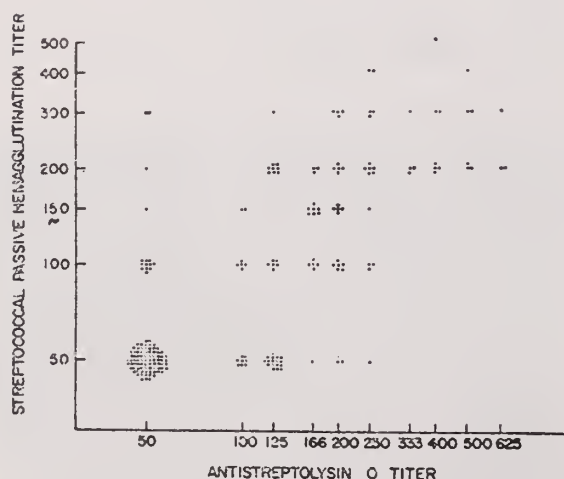


Fig. 15: Correlation between streptococcal passive hemagglutination test and antistreptolysin O titer.

in rheumatic fever are the anti-heart antibodies (Figure 16) that can be demonstrated, as in this case, by immunofluorescence. A section of normal heart is used as the substrate; on this section is put a drop of the serum of the patient, or a dilution thereof; after washing, a fluorescein-conjugated rabbit antibody against human gammaglobulin is added. This will stick, and therefore will show later as a 'bright' spot only where the human gammaglobulin of the patient's serum had previously stuck. With this technique it is possible to demonstrate heart antibodies (Figure 17), which have some degree of specificity

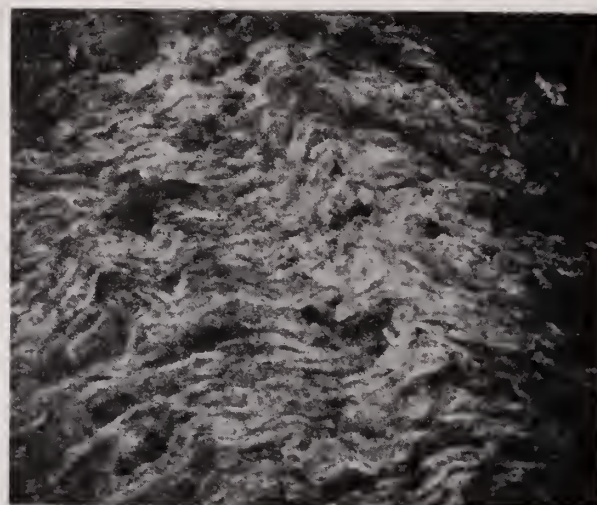


Fig. 16: Immunofluorescent pattern obtained by layering the serum of a patient with rheumatic fever on a normal heart section, washing, and then staining the preparation with fluoresceinated rabbit antibody against human gammaglobulin. The light areas indicate fluorescence due to local fixation of human gamma globulin — presumably anti-heart antibodies.

for rheumatic fever (9). The degree of specificity and of sensitivity vary with the details of technique and the various populations of patients. Whether the determinations of anti-heart antibodies will become a useful addition to the diagnostic armamentarium remains to be seen.

## Part Two: Prevention

Years ago the main emphasis of the American Heart Association and other health agencies interested in rheumatic fever control was on secondary prophylaxis — the prevention of rheumatic fever recurrences. This has the advantage of dealing with a defined and limited population and of being quite effective — at least when injectable benzathine penicillin is used. More recently, there has been an increase of interest in primary prevention — since secondary prevention, by its very nature, cannot eradicate rheumatic fever. All it can do is to stop rheumatic patients at the first attack — a remarkable success no doubt, but not one that will necessarily prevent progression of heart disease. That primary prophylaxis is effective — provided

## INCIDENCE OF ANTI-HEART ANTIBODIES

	No. of Patients	Percent Positives
Acute rheumatic fever	171	41.5
Acute rheumatic carditis	71	63.4
Inactive rheumatic fever	201	16.4
Rheumatic heart disease, post-cardiotomy	19	63.1
Heart disease, non-rheumatic	39	6.3
Acute glomerulonephritis	26	7.7
Rheumatoid arthritis and other collagen diseases	40	0.0
Healthy controls	66	3.0

Fig. 17: *Percentage of positive anti-heart antibody tests in patients with various diseases and healthy controls.*

## PREVENTION OF FIRST ATTACKS OF RHEUMATIC FEVER \*

	No. of Rheumatic Fever Attacks
1,178 patients with exudative streptococcal pharyngitis treated with an "eradicating dose" of penicillin	2
1,162 patients like the above, but not treated	28

\* - L. W. Wannamaker et al., 1951

Fig. 18: *A controlled study on the prevention of rheumatic fever in a military population.*

that penicillin is administered in such a way as to obtain effective blood levels for at least 10 days — was shown by Wannamaker and others more than 25 years ago (Figure 18) in a very clear-cut clinical trial, whereby the treated group had only 1/10 the rheumatic fever attacks of the untreated group (10).

How is it then that rheumatic fever is still around? Figure 19 provides a partial answer, through retrospective analyses of prevention failures, that is, of patients who developed rheumatic fever. Of 100 patients so afflicted, up to 1/3 remember no preceding upper respiratory infection; another third remember a preceding infection for which, however, they did not seek medical attention; and a last third

had consulted a doctor for their preceding infection, but the infection in most cases had not been properly diagnosed or treated. Now, what can be done? The first group is generally considered beyond salvage. Yet, many of these asymptomatic patients could have been reached through their symptomatic contacts. It is well known that in the families of patients who come to medical attention with streptococcal pharyngitis, one very often finds siblings with asymptomatic streptococcal infections—i.e., a positive throat culture without symptoms. Treatment of such contacts is an effective way of getting at this first group of prophylaxis failures.

The second group is the one that can be helped

## FAILURES TO PREVENT RHEUMATIC FEVER

Of 100 patients who develop rheumatic fever:

13-33 percent remember no preceding symptomatic infection.

31-33 percent remember a preceding symptomatic infection for which they did not see a doctor.

30-56 percent had consulted a doctor for a preceding respiratory infection.

(Data from various investigators)

Fig. 19: Why rheumatic fever is still around: analyses of the antecedents of rheumatic fever attacks.

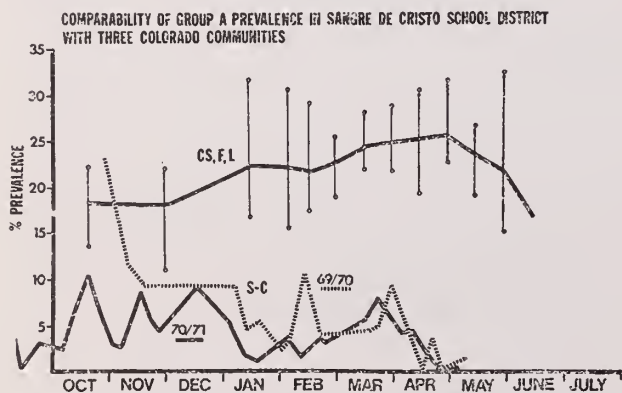


Fig. 20: Streptococcal isolation rates of a "treated" community (Natrona County) and of three untreated communities (Frisco, Loveland, and Colorado Springs). For definition of "treatment" see text. (Phibbs et al., courtesy of JAMA).

the most by greater availability of medical services. It is not only a question of money; even if a service is free, like a clinic or an emergency room, it may not be used, especially for a seemingly minor ailment, like a sore throat, if the waiting line is too long or the clinic too far away.

The third group can be helped through medical

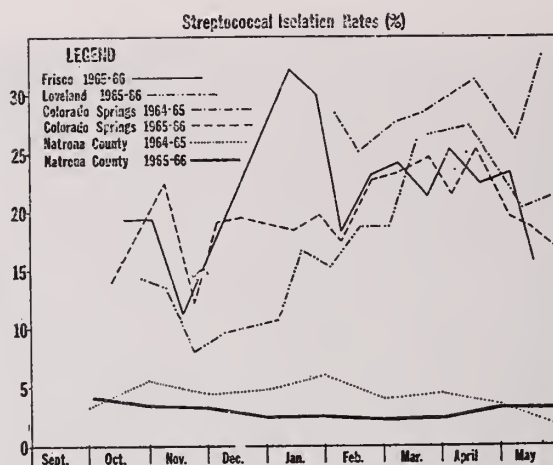


Fig. 21: Streptococcal isolation rates in a "treated" school community (SC) and in three untreated communities (CS, F, L.) (Zimmerman et al., courtesy of Pediatrics).

education and through better and less expensive laboratory services. I mean particularly throat cultures, which are essential for an accurate diagnosis of streptococcal pharyngitis, and that too often, in too many localities are either unavailable or too expensive. One must remember in this connection that there is no need to determine all the various innocuous bacterial species that may be found on a throat culture — the important question is whether we have a beta-hemolytic strep, not a *neisseria catarrhalis*. By the same token, since group A beta-hemolytic strep is regularly sensitive to penicillin, there is no point in determining its sensitivity to various antibiotics. By cutting out these determinations, one may decrease the cost of the throat culture (11).

One of the ways in which all these "remedies" can be brought together is by primary prevention programs based or centered in the school. After all, rheumatic fever and streptococcal infections occur so frequently among school children that the school itself is the best access to the susceptible population. Moreover, around a school it may be possible to mobilize volunteers — concerned mothers who can take throat cultures and screen the children for sore throats. Finally, since strep infections are communicable diseases, one can enforce treatment by denying readmission to sick children until they have been treated, or until their throat cultures have reverted to negative.

The best known of these programs is that devised by Dr. Brendan Phibbs in Wyoming, in which children



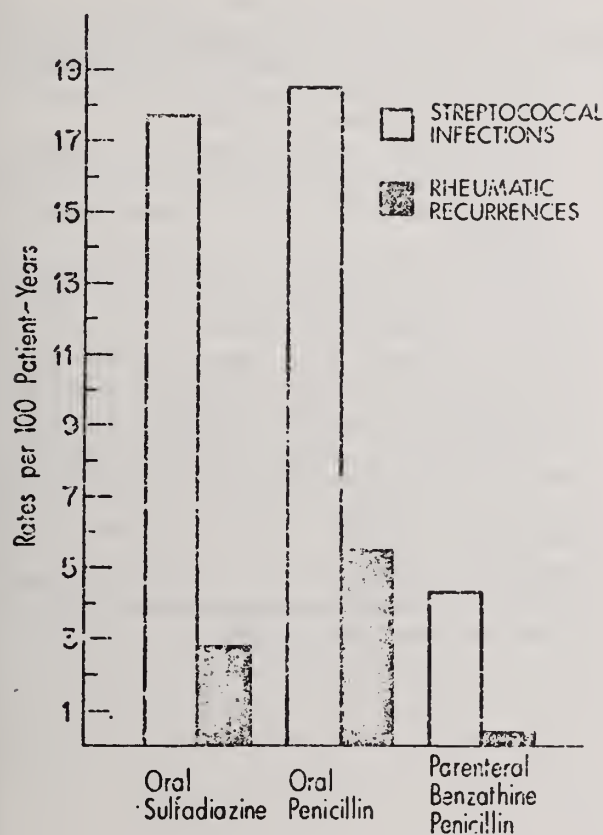


Fig. 22: Streptococcal infections and rheumatic fever recurrence rates in comparable patients receiving oral sulfadiazine, oral penicillin, or parenteral benzathine penicillin. From data in ref. 14. (Taranta & Gordis, courtesy of Cardiovasc. Clin.).

are asked every morning whether they have a sore throat or a cold (12). Those who answer yes and those who are just returning from being sick at home have their throat culture taken. In addition, the volunteers inspect the throat of all the children once a week — since children and, especially, small children, may have a fiery red throat and yet may not complain of soreness in the throat. For processing of the throat cultures, the State laboratory is used, and the parents of the children with group A streptococci in their throats are notified and treatment is requested. This kind of program is effective in bringing down the streptococcal prevalence rate, i.e., the percent of positive throat cultures, as shown in Figure 20, where the prevalence rates of a treated community are compared with those of 3 control untreated communities. Even more convincing are the data shown in Figure 21 where the percent of positive throat cultures is given over the school year

before and after a streptococcal monitoring program was started, and in control schools (13). This kind of program is expected to bring down the attack rate of rheumatic fever and glomerulonephritis in the community, although this is more difficult to prove, due to the low attack rate of these diseases. Nevertheless, Phibbs has presented evidence that his protected, primary school population escaped a rheumatic fever epidemic that affected the remainder of the population (12).

As for secondary prevention, for all its lack of glamour and its limited promises, it works, it's needed and it's relatively cheap. In a large study completed a few years ago at Irvington House, the rheumatic recurrences in children on parenteral benzathine penicillin were about 1/10 of those on oral penicillin, (14) (Figure 22). This was in a highly susceptible population, studied within five years of their latest rheumatic attack. These recurrence rates will vary with the population studied and with the intensity of the streptococcal challenge.

No discussion of prevention would be complete without a mention of the vaccine. Although theoretically attractive, its application is delayed by a series of snags. Since immunity is type-specific there may be a need for too many vaccines — too complicated for the chemist, too burdensome perhaps for the host's immune system. Moreover, the M-protein preparations, even those most purified, are quite toxic to all but the youngest, though the intranasal route may circumvent this snag. Finally, a report of Massell's group a few years ago presented data suggestive of a possible rheumatogenic effect of a streptococcal vaccine (15). Therefore the vaccine may or may not come into general use. In either case, fortunately the disease may be controlled largely with the available means. Whether rheumatic fever sticks around or disappears is largely up to us.

## References

1. Taranta, A., and Moody, M.: Diagnosis of streptococcal pharyngitis and rheumatic fever. *Pediatr. Clin. North Am.* 18: 125, 1971.
2. Markowitz, M., Stollerman, G. H., Taranta, A., et al: Jones criteria (revised) for guidance in the diagnosis of rheumatic fever. *Circulation* 32: 665, 1965.
3. Feinstein, A. R., Taranta, A., and DiMassa, R.: Errors in the diagnosis of acute rheumatic fever. *N. Y. State J. Med.* 60: 2835, 1960.
4. Stollerman, G. H., Lewis, A. J., Schultz, I., et al: Rela-

- tionship of immune response to group A streptococci to the course of acute, chronic, and recurrent rheumatic fever. *Am. J. Med.* 20: 163, 1956.
5. Taranta, A., and Stollerman, G. H.: The relationship of Sydenham's Chorea to infection with group A streptococci. *Am. J. Med.* 20: 175, 1956.
  6. Bernhard, G. C., and Stollerman, G. H.: Serum inhibition of streptococcal diphosphopyridine nucleotidase in uncomplicated streptococcal pharyngitis and in rheumatic fever. *J. Clin. Invest.* 38: 1942, 1959.
  7. Ayoub, E., and Wannamaker, L. W.: Streptococcal antibody titers in Sydenham's chorea. *Pediatrics* 38: 946, 1966.
  8. Janeff, J., Janeff, D., Taranta, A., et al: A screening test for streptococcal antibodies. *Lab. Med.* 2: 38, 1971.
  9. Hess, E. V., Fink, C. W., Taranta, A., et al: Heart muscle antibodies in rheumatic fever and other diseases. *J. Clin. Invest.* 43: 886, 1964.
  10. Wannamaker, L. W., Rammelkamp, C. H., Jr., Denny, F. W., et al: Prophylaxis of acute rheumatic fever by treatment of the preceding streptococcal infection with various amounts of depot penicillin. *Am. J. Med.* 10: 673, 1951.
  11. Rheumatic Fever and Rheumatic Heart Disease Study Group, Intersociety Commission for Heart Disease Resources (A. Taranta, chairman; members: J. Fiedler, C. Frank, B. S. Gilson, L. Gordis, C. Hufnagel, M. Markowitz, L. W. Wannamaker) Prevention of rheumatic fever and rheumatic heart disease. *Circulation* 41: A-1, 1970.
  12. Phibbs, B., Taylor, J., and Zimmerman, R. A.: A community-wide streptococcal control project. The Natrona County primary prevention program, Casper, Wyoming. *JAMA* 214: 2018, 1970.
  13. Zimmerman, R. A., Biggs, B. A., Bolin, R. A. et al: An effective program for reducing group A streptococcal prevalence. *Pediatrics* 48: 566, 1971.
  14. Wood, H. F., Feinstein, A. R., Taranta, A. et al: Rheumatic fever in children and adolescents. A long-term epidemiologic study of subsequent prophylaxis, streptococcal infections, and clinical sequelae. III. Comparative effectiveness of three prophylaxis regimens in preventing streptococcal infections and rheumatic recurrences. *Ann. Intern. Med.* 60 (Feb. Suppl.): 31, 1964.
  15. Massell, B. F., Honikman, L. H., and Amezcua, J.: Rheumatic fever following streptococcal vaccination. Report of three cases. *JAMA* 207: 1115, 1969.

## DIARREA Y COLITIS ASOCIADA A ANTIBIOTICOS

Carlos H. Ramírez Ronda, MD, FACP

Carlos León-Valiente, MD

Los efectos secundarios asociados a los antibióticos ocurren más frecuentemente de lo que creemos. Notamos una multiplicidad de síntomas secundarios a la ingestión de antibióticos. Entre los más comunes se encuentran los relacionados al tracto gastrointestinal tales como: anorexia, náusea, vómitos, molestias epigástricas, sensación de llenura, dolores abdominales asociados a retortijones, excreta líquida, diarrea, pruritus anal e irritación perineal. La mayor parte del tiempo estos síntomas están relacionados a la cantidad de antibióticos usados. En los próximos párrafos discutiremos un efecto común de los antibióticos, la diarrea y luego enfocaremos en uno potencialmente serio: el desarrollo de colitis y colitis pseudomembranosa.

### Diarrea

Virtualmente todos los antibióticos son capaces de producir diarrea. Dado ciertas condiciones, la incidencia de diarrea severa varía de acuerdo con los antibióticos específicamente usados. Además, la condición del paciente tal como su salud general, su flora normal y la ecología bacteriana local juega un papel importante.

Cuando estudiamos la diarrea post antibióticos nos encontramos con una enfermedad que tiene un espectro amplio desde diarrea leve a colitis pseudomembranosa con megacolon tóxico. Afortunadamente la parte leve del espectro es la que más comunmente encontramos (1).

Para poder analizar las diarreas post antibióticas

tenemos que definir las en términos de los síntomas y patología: la diarrea leve no específica asociada con cambios en la microflora, la diarrea asociada con proliferación de organismos resistentes y la malabsorción inducida por antibióticos. Afortunadamente, la incidencia clínica es en proporción inversa a la severidad de la enfermedad.

### Diarrea Leve No Específica

Esta diarrea está usualmente asociada con anorexia, náusea, vómitos y pruritus anal. Los antibióticos tales como la eritromicina, tetraciclina, ampicilina, lincomicina, clindamicina y neomicina usualmente se incriminan (1). La etiología del síndrome no está clara y algunos investigadores han sugerido una alteración en la flora intestinal normal. Cuando el antibiótico se administra parenteralmente usualmente hay menos diarrea y síntomas gastrointestinales. Prácticamente todos los pacientes responden bien una vez se discontinúa el uso del antibiótico.

### Diarrea con Proliferación de Organismos Resistentes

Cuando el uso de antibióticos de amplio espectro resulta en crecimiento de cepas bacterianas resistentes o de sobrecrecimiento de hongos, el paciente, puede desarrollar una diarrea explosiva. Entre los organismos que más comunmente se proliferan están *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Proteus*, *Streptococcus faecalis*, *Candida* y *Salmonella* (1, 2). Al encontrar este problema se procede con una tinción de excreta con tinción de gram y un cultivo de esta. Si la tinción revela cocos gram positivos en grumos y se confirma por cultivo la presencia de *Staphylococcus aureus* usted debe de sospechar enterocolitis estafilocócica y debe proceder a hacer una

---

De los Departamentos de Investigación y Medicina, Hospital de Veteranos y Escuela de Medicina, Universidad de Puerto Rico, San Juan, P. R.

Copias de este artículo se pueden adquirir escribiendo a: Dr. Carlos H. Ramírez Ronda, Laboratorio de Enfermedades Infecciosas, USD, Hospital de Veteranos, GPO Box 4867, San Juan, Puerto Rico 00936.



**TABLA I**  
**DIAGNOSTICO DE COLITIS ASOCIADA A ANTIBIOTICOS**

1. Piense en colitis en un paciente recibiendo antibióticos que desarrolle fiebre, diarrea, tenesmo, etc.
2. Descontinúe el antibiótico.
3. Tome muestra de excreta para: tinción de gram, cultivo, examen de coprología y sangre oculta.
- 4 a. Si los síntomas persisten:
  - a. Proctosigmoidoscopia
  - b. Biopsia de la mucosa
  - c. Enema de bario
- 4 b. Si la tinción de gram demuestra gram positivo y/o el cultivo demuestra un crecimiento puro de estafilococos:
  - a. Proctosigmoidoscopia
  - b. Comience Vancomicina oral
  - c. Comience con una penicilina resistente a penicilinas

**TABLA II**  
**MANEJO DE COLITIS PSEUDOMEMBRANOSA ASOCIADA A ANTIBIOTICOS**

1. Comience con enemas de corticoesteroides y/o corticoesteroides sistémicos (Prednisona 40-60 mg/día)
2. Considere Colestiramina
3. Siempre:
  - a. Mantenga el balance de líquidos y electrolitos
  - b. Observe la hemoglobina
4. Esté atento a:
  - a. Megacolon tóxico

proctosigmoidoscopia para eliminar esta posibilidad. Si se encuentra una pseudomembrana y otros cambios no específicos compatibles con enterocolitis estafilocócica el tratamiento debe ser agresivo y rápido. Recomendamos el uso de vancomicina oral 0.5 gms cada 6 hrs. y el uso de una penicilina resistente a penicilinas parenteralmente como metilina o nafcilina de 8-12 gramos endovenosas al día en dosis cada 4 horas. Si la diarrea es causada por cualquier otro agente bacteriano, el tratamiento difiere en que solamente con usted discontinuar el antibiótico de amplio espectro, el cuadro clínico mejora y se resuelve solo.

El papel de la flora normal en la prevención de sobrecrecimiento de patógenos resistentes se ha demostrado. Por ejemplo, cuando un paciente es pretratado con estreptomina o neomicina su susceptibilidad a

*Salmonella typhosa* aumenta. El antibiótico suprime la flora indígena incluyendo organismos anaeróbicos que producen ácidos volátiles grasos como acético y butírico que son bactericidas e inhiben el crecimiento de patógenos potenciales.

### Diarrea Debido a Toxicidad Intestinal

El uso de un antibiótico puede causar esta condición que ocurre en algunos pacientes cuyas manifestaciones clínicas incluyen diarrea, flatulencia, excreta grasosa, náusea y ocasionalmente vómitos. Los efectos tóxicos directos se ven cuando los hidroclouros de

tetraciclina son usados. A pesar de ser esta preparación más soluble, forma unas soluciones ácidas fuertes las cuales tienen efectos irritantes locales en la mucosa intestinal resultando en el cuadro clínico descrito. Un segundo ejemplo es el de neomicina y kanamicina los cuales causan malabsorción, creando un defecto en la hidrólisis de triglicéridos de cadenas largas, probablemente por inhibición de la lipasa pancreática o alteración en la de conjugación de sales biliares. El tratamiento es descontinuar el uso de antibióticos y comenzar tratamiento sintomático.

### Colitis Pseudomembranosa Asociada a Antibióticos

El término colitis pseudomembranosa incluye una serie de condiciones de variada etiología tales como: complicaciones de isquemia gastrointestinal, complicación post cirugía gastrointestinal, shock, enfermedades debilitantes, hipoperfusión focal del intestino, uremia, sobrecrecimiento de estafilococos y uso de antibióticos de amplio espectro. Por muchos años el síndrome ha sido reportado como una complicación post antibiótica en donde se ha incriminado a las tetraciclinas, cloranfenicol, penicilina, ampicilina, lincomicina y clindamicina.

La colitis asociada a antibióticos ha recibido muchos nombres que incluyen enterocolitis antibiótica, enterocolitis estafilocócica y colitis pseudomembranosa. Más debemos de conocer que no todas las colitis asociadas a antibióticos han sido asociadas con un sobrecrecimiento de organismos y no todas las colitis pseudomembranosas han recibido la misma descripción patológica (1, 2, 3).

La lincomicina y clindamicina se han reportado estar asociadas con colitis en un número significativo de pacientes desde 1973. La frecuencia de esta complicación es más alta que la que se ve con la mayor parte de los otros antibióticos. La entidad se ha llamado "Colitis por Clindamicina" pero muchos autores, incluyéndonos, preferimos el término de "Colitis Asociada a Clindamicina" ya que no queremos implicar una relación directa entre causa y efecto (4, 5, 6).

### Colitis Asociada a Clindamicina

La colitis asociada a clindamicina fue reportada

por primera vez en 1973 por Cohen. Anterior a esto Kaplan y Weinstein describieron una entidad que simulaba a la colitis ulcerativa aguda en pacientes que estaban tomando grandes dosis orales de lincomicina, especialmente si el paciente continuaba tomando la medicina una vez la diarrea comenzaba.

Desde 1973 han surgido una serie de reportes de este síndrome en pacientes que han estado tomando clindamicina en muchas partes de los E. U. y en otras partes del mundo incluyendo un estudio prospectivo por Tedesco en 1975 (5). La colitis asociada a clindamicina es una colitis pseudomembranosa no estafilocócica (4, 5, 6, 7).

### Incidencia

En un estudio prospectivo de 200 pacientes consecutivos recibiendo clindamicina en el Hospital Barnes en St. Louis, Tedesco demostró una incidencia acumulativa de diarrea de 21 por ciento, definida como un cambio en los hábitos del intestino que llevaban a por lo menos más de 5 movimientos diarréicos por día y una incidencia acumulativa de 10 por ciento de colitis pseudomembranosa (5). La incidencia según reportada por el manufacturero es de 1:100,000 casos tratados pero la incidencia calculada por uno de los autores en el área de Dallas es de 1 en 5,000 a 1 en 10,000 (7, 8).

### Sintomatología

Típicamente el paciente que desarrolla colitis asociada a clindamicina ha estado tomando el antibiótico por 4 a 6 días por vía oral o parenteral. Su condición se caracteriza por el desarrollo de fiebre, leucocitosis, retortijones abdominales, distensión abdominal, tenesmus, diarrea que puede estar acompañada por sangre, pus o moco. El paciente puede tener de 10 a 20 deposiciones de excreta al día, más en algunos pacientes estos síntomas no se desarrollan hasta dos semanas después de haber cesado el tratamiento. Algunos pacientes pueden tomar clindamicina en una ocasión sin dificultad para luego desarrollar colitis durante un tratamiento subsiguiente. Las mujeres son más frecuentemente afectadas que los hombres en una razón de 4 a 1. Los pacientes en los cuales la colitis asociada a clindamicina ha ocurrido más frecuentemente están en los grupos de edades de 20 a 39 años y de 50 a 69

años. La severidad y manifestaciones varían desde una gastroenteritis menor a un cuadro severo de fiebre, prostración, deshidratación y megacolon tóxico que puede resultar y ha sido letal en algunos pacientes. Hay un reporte de colitis pseudomembranosa familiar en donde un niño y su padre desarrollan colitis después de recibir lincomicina, el compuesto del cual se deriva la clindamicina. Ya que puede haber un defecto genético en algunas familias y hasta que la importancia relativa del riesgo genético se establezca debe de prescribirse cuidadosamente antibióticos, especialmente clindamicina, a familiares de individuos con historial de haber tenido un episodio de colitis pseudomembranosa.

La colitis asociada a clindamicina puede presentarse como una condición quirúrgica aguda del abdomen con fiebre, leucocitosis, dolor abdominal severo y dolor a la palpación.

La proctoscopia demuestra una mucosa edematosa e hiperémica que puede o no demostrar friabilidad, la presencia de placas, color crema sobre una base eritematosa, una membrana completa o una combinación de estas. Los hallazgos principales son hiperemia, edema y una cantidad moderada de friabilidad o granularidad, ninguna de las cuales es específica para el diagnóstico de colitis pseudomembranosa y puede parecerse al cuadro de colitis ulcerativa. Las lesiones en placa varían en tamaño de 1 a 5 mm y ocasionalmente son confluentes, son color amarillo blanqueco y frecuentemente e inicialmente cubiertas por un moco grueso. Se ha correlacionado el tamaño de las placas y la intratabilidad o falta de respuesta de la diarrea a todas las formas de terapia médica.

La biopsia de mucosa rectal demuestra una pseudomembrana con inflamación de la mucosa rectal. El epitelio superficial usualmente se encuentra necrosado, más cuando se encuentran úlceras no hay evidencia de vasculitis o trombosis. La pseudomembrana puede adherirse a la mucosa, pero frecuentemente se observa que se separa. La biopsia de la placa de la pseudomembrana no siempre demuestra un cuadro patológico característico. Se compone de leucocitos polimorfonucleares, fibrina y desechos epiteliales; se ve un número aumentado de células globosas y hay áreas que tienen necrosis epitelial y erosión.

El examen del colon por enema de bario durante el episodio agudo de colitis puede demostrar cambios que varían desde cambios no específicos a un patrón serrado en la mucosa. Algunos autores han sugerido que el estudio del colon con enema de bario debe de llevarse a cabo con contraste de aire para determinar

la presencia de placas o pseudomembranas en la mucosa, pero este procedimiento no tiene el mismo rendimiento que una proctosigmoidoscopia.

Las pruebas de laboratorio pueden revelar leucocitos, desbalance electrolítico, hipoproteinemia y anemia. Los estudios bacteriológicos característicamente demuestran la ausencia de patógenos y nunca se ha demostrado el sobrecrecimiento de ningún organismo. El examen de la excreta para huevos y parásitos es usualmente negativo. A pesar de que los estudios bacteriológicos y coprológicos son usualmente negativos esto no debe precluir la importancia de llevarlos a cabo en todo paciente con colitis, esté o no asociada a antibióticos.

## Diagnóstico

El diagnóstico de la colitis asociada a clindamicina o cualquier colitis asociada a antibióticos está basada primeramente en que el médico sepa que puede ocurrir. Debe de sospecharse colitis asociada a clindamicina en cualquier mujer joven o mujer de edad madura que desarrolla diarrea después de tomar el antibiótico por 3 a 5 días. Una vez se sospecha colitis asociada al antibiótico, este debe de discontinuarse y un examen de excreta incluyendo cultivo, examen para huevos y parásitos, sangre oculta y tinción de gram debe llevarse a cabo. Si los síntomas persisten más de 24 a 48 hrs. o si el paciente se deteriora clínicamente por cualquier razón un examen proctosigmoidoscópico con biopsia de la mucosa debe de llevarse a cabo. Si se encuentra la presencia de una pseudomembrana durante el examen sigmoidoscópico, se recomienda tratamiento agresivo.

## Manejo

Una vez se sospecha la colitis asociada a antibióticos, el antibiótico debe de discontinuarse.

La terapia antibiótica está contraindicada a menos que ocurra una infección secundaria. Nosotros no recomendamos el uso de opiáceos, anticolinérgicos o Lomotil®, ya que estas drogas pueden prolongar el contacto entre el antibiótico y la mucosa del intestino y exacerbar o prolongar los síntomas.

Si se desea usar una preparación antidiarreica, recetar una mezcla de kaolina y pectina está indicado, ya que esta preparación parece ser benigna. Hay evidencia



reciente del tratamiento efectivo de varios pacientes con colitis asociada a antibióticos con colestiramina y su uso en estos casos debe de considerarse. El manejo cuidadoso de los líquidos, electrolitos y la tasa de proteína es muy importante. Trate la colitis agresivamente utilizando corticoesteroides parenterales u orales y enemas de corticoesteroides. Es imperativo recordar que si el paciente no es tratado adecuadamente puede desarrollarse una colitis de extrema seriedad con megacolon tóxico y/o perforación colónica, requiriendo colectomía en algunos casos y ocurriendo muerte en otros. No debemos de olvidarnos de que esta condición puede confundirse con el abdomen quirúrgico.

### Medidas Preventivas

La mayor parte de los pacientes que han desarrollado esta complicación han usado clindamicina para una condición relativamente benigna. A pesar de que la incidencia de colitis es rara, su seriedad potencial apunta a que el uso de clindamicina en adultos debe ser limitado a infecciones severas en donde agentes potencialmente menos tóxicos no se encuentren. Estas infecciones son primariamente aquellas en donde el organismo anaeróbico *Bacteroides fragilis* es posiblemente la causa de la infección, como es tromboflebitis séptica post-parto o post-aborto, aborto séptico, absceso del hígado, peritonitis y sinusitis anaeróbica crónica. Debemos mencionar que aunque la colitis asociada a clindamicina se ve con ambas formas de administración (oral y parenteral), la incidencia aparentemente es menor cuando la forma parenteral es usada. ¿Por qué la clindamicina produce colitis? No sabemos su patofisiología. No se explica adecuadamente por cambios en la microflora del intestino, por cambios electrolíticos, por cambios de ácidos biliares o por efecto directo irritante por la droga o uno de sus metabolitos. Se ha sugerido la posibilidad de que la droga o sus metabolitos se acumulan en el epitelio de la mucosa intestinal resultando en disminución de la síntesis de proteína localmente provocando ulceraciones y la formación de membranas.

### Otros Antibióticos y Colitis Pseudomembranosa

A través de los años se han descrito una serie de

casos de colitis pseudomembranosa y proctitis asociada a antibiótico tales como aureomicina, tetraciclinas, cloranfenicol, penicilina y ampicilina. A pesar de que la entidad fue descrita hace más de 25 años la frecuencia y morbilidad han sido tan bajas que nuestros conocimientos sobre la condición han sido limitados. No fue hasta 1973 que la colitis asociada a clindamicina trajo nuevo interés en el estudio de la colitis asociada a antibióticos. Por alguna razón la clindamicina está asociada con diarreas y colitis más frecuentemente que otros antibióticos. Este nuevo interés en colitis asociada a antibióticos llevó a otros estudios prospectivos. Por ejemplo, Tedesco recientemente ha completado un estudio prospectivo de síntomas gastrointestinales asociados a ampicilina (9). El encontró una incidencia de diarreas de 4.5 por ciento sin la presencia de colitis pseudomembranosa. En el momento se estudian otros antibióticos. Esperamos que sus resultados nos hagan más conscientes de los efectos secundarios que vemos con antibióticos y nos ayuden a prescribir estos agentes más apropiadamente. Esperamos que esta discusión ayude al médico a obtener un cuadro más claro del estado actual de la diarrea asociada a antibióticos y que le ayude a reconocer más frecuentemente esta condición ya que es potencialmente seria.

### Referencias

1. Fekerty, R. F.: Gastrointestinal complications of antibiotic therapy. JAMA 203: 210-212, 1968.
2. Valberg, L. S., Truelove, S. C.: Noninfective pseudomembranous colitis following antibiotic therapy. Ann J Dig Dis 5: 728-738, 1960.
3. Reiner, L., et al: Pseudomembranous colitis following aureomycin and chloramphenicol. Arch Pathol 54: 39-66, 1952.
4. Le Froek, J. L., et al: The spectrum of colitis associated with lincomycin and clindamycin therapy. J Infect Dis 131: S108-S115, 1975.
5. Tedesco, F. J., et al: Clindamycin-associated colitis: A prospective study. Ann Intern Med 81: 429-433, 1974.
6. Tully, T. E., Feinberg, S. B.: A reappearance of antibiotic induced pseudomembranous enterocolitis. Radiology 110: 563-567, 1974.
7. Ramírez-Ronda, C. H., Sanford, J. P.: Clindamycin: A trojan horse? Arch Otolaryngol 101: 235-237, 1975.
8. Ramírez-Ronda, C. H.: Letter: Incidence of clindamycin-associated colitis. Ann Intern Med 81: 860, 1974.
9. Tedesco, F. J.: Ampicillin-associated diarrhea: A prospective study. Am J Dig Dis 20: 295-297, 1975.

# SINDROME DE LAURENCE-MOON-BIEDL-BARDET.

## A propósito de un caso

Adolfo Pérez Comas, MD, PhD

J. Z. Laurence y R. C. Moon (1) describieron en 1865 un síndrome caracterizado en su forma completa por obesidad, retardación mental, polidactilia, retinis pigmentosa e hipogenitalismo. En 1920, Bardet y Biedl (2) popularizaron y delinearon las características clínicas de la condición. Se trata de una afección hereditaria autosómica recesiva que, aunque rara, ha sido informada aproximadamente 300 veces en la literatura mundial. Existe una gran variabilidad en la presentación de los caracteres clínicos, no estando presentes todas las características en un caso en particular (3).

En el año 1972 evaluamos en nuestro consultorio una niña con caracteres que sugerían esta condición, presentando además coloboma del iris, hallazgo no informado previamente que motiva esta presentación.

### Descripción del Caso

E. M. F. nació a término de una madre de 19 años grávida 11 para 11 Ab O y un padre de 37 años de edad. La gestación fue normal y no complicada, presentándose con un peso al nacer de 9 libras y 22 pulgadas de longitud. Presentó cianosis, la cual se resolvió sola, observándose además, polidactilia con sindactilia cutánea en el pie derecho y coloboma inferior del iris en el ojo derecho. A los 7 años de edad le fue amputado el dedo extra del pie derecho.

Hasta donde los padres recuerdan, la niña ha sido obesa. Su desarrollo psicomotor siempre fue retrasado. A los 13 años de edad no sabe vestirse bien, no controla voluntariamente (en ocasiones) la micción, y su vocabulario no es muy extenso. A pesar de ello ha pasado de grado (hasta 5to. grado) con calificaciones muy bajas. Presenta problemas con la visión nocturna y aún de día no ve bien y tropieza.

A los 10 años de edad presentó su menarquía, teniendo sucesivamente 2 períodos mensuales de un día de duración hasta los 13 años cuando la regla vuelve a aparecer irregular y anárquica.

Su evaluación psicométrica mediante las pruebas de "Escala de inteligencia Weschler para niños", "dibujo de la figura humana" y "prueba Gestáltica Visomotora", mostró que presenta retardación leve con una edad mental de 7 años y un cociente intelectual de 53.

Al examen físico nos presenta un peso de 159 libras (por ciento 97), una talla de 61 pulgadas (por ciento 50) y una circunferencia cefálica de 22 pulgadas. Su obesidad es genera-



Fig. 1: Aspecto general de la paciente. Obsérvese obesidad generalizada.



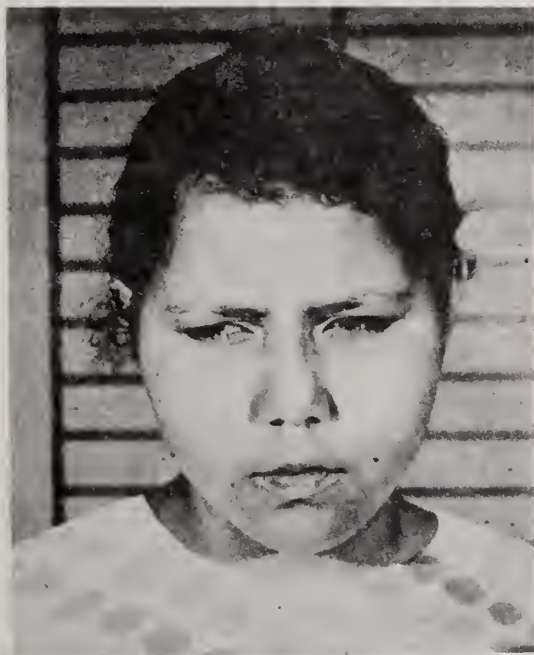


Fig. 2: Fotografía de cara donde se observa estrabismo divergente y ligera asimetría facial.



Fig. 3: Coloboma del iris en ojo derecho.

lizada (figura 1) con pigmentación marrón y piel reseca en el cuello (acantosis) debido al roce y a la obesidad. Presenta estrabismo divergente y ligera asimetría facial (figura 2). Se observa, además, coloboma inferior del iris en el ojo derecho (figura 3). El fondo de ojo presenta retinitis pigmentaria, más marcada en el ojo izquierdo, con palidez de ambos

discos y ausencia del reflejo macular. El sistema cardiorespiratorio es normal y no presenta organomegalia abdominal. Su desarrollo puberal está en la etapa de tanner 3 \*. Sin vello axilar. Sus manos y pies son grandes mostrando un predominio de espirales (8 espirales y 2 bucles cubitales) en los dedos de las manos y ángulos atd de las palmas de las manos normales.

## Discusión

A mediados del siglo pasado Laurence y Moon (1) pudieron encuadrar una serie de características que se presentan más o menos acordes en una serie de pacientes, bajo el síndrome hoy conocido como de Laurence-Moon Biedl-Bardet. Se trata de una afección de caracteres algo variables, que se transmite con herencia mendeliana autosómica recesiva (6-7).

Los caracteres fundamentales del síndrome son: obesidad (83 por ciento), retardación mental (80 por ciento), polidactilia, sindactilia o ambas (75 por ciento), retinitis pigmentosa (68 por ciento), hipoplasia genital, hipogonadismo o ambos (60 por ciento) (2). El grado de anormalidad puede variar considerablemente entre los hermanos afectados, haciéndose, en ocasiones, difícil el diagnóstico en un caso aislado que presente parcialmente las características del síndrome (3).

Debido a la gran variabilidad en la presentación de las características Klein y Amman (8) clasifican la condición en varias formas: 1) formas completas donde están presentes los caracteres fundamentales, 2) formas incompletas donde uno o dos de los caracteres cardinales están ausentes, 3) formas abortivas donde uno o dos de los caracteres están presentes, 4) formas atípicas, donde la retinitis pigmentosa está ausente y es reemplazada por otros trastornos oculares, como atrofia óptica, miopía, oftalmoplegía, etc., y 5) formas extensivas, donde además de los hallazgos cardinales existen otros defectos congénitos importantes asociados.

La obesidad está presente en un 81-95 por ciento de los pacientes, usualmente comienza en la niñez y aumenta con la edad. La polidactilia puede ser el único hallazgo al nacer, usualmente es postaxial. Cuando no se observa polidactilia al examen físico, un examen radiológico de las extremidades suele mostrar

\* vello púbico negro, grueso y rizado. Areolas y pecho agrandado, pero sin separación de los contornos.



anomalías, mayormente del quinto dedo de la mano. La retinitis pigmentosa está presente en un 15 por ciento de los pacientes si tomamos en cuenta las formas atípicas, abortivas, etc. Los pacientes pueden presentar otras anomalías oculares. A los 20 años el 75 por ciento de los pacientes han perdido la visión. El hipogenitalismo es más frecuente en los varones. La retardación mental suele estar presente en un 70-85 por ciento de los casos y puede variar de leve a severa. En algunos pacientes se observa la retardación desde temprana infancia, pero otros pueden presentar un desarrollo aparentemente normal hasta los 7-8 años (8, 9).

Se conocen otros defectos menos frecuentes, como son: defectos renales (incluyendo lesiones de glomerulonefritis crónica); sordomudez (30 veces más frecuente que en la población normal), nistagmus, estrabismo, atrofia óptica, clinodactilia del quinto dedo, defectos cardíacos variables incluyendo tetralogía de Fallot, hipospadias, atresia anal y aunque no de forma consistente, estatura corta (2, 8, 9).

El infantilismo sexual, la obesidad, la baja estatura y la diabetes insípida se cree que son debidas a un defecto congénito del hipotálamo (3, 4).

La retinitis pigmentosa da lugar, generalmente, a problemas de la visión crepuscular, aún a pequeña edad. El retinograma es anormal y puede ser útil en el diagnóstico. Puede haber afectación de nervios craneales o de degeneración espino-cerebelosa (2). Los casos que presentan infantilismo sexual tienen una disminución en la excreción urinaria de gonadotrofinas (3). La biopsia testicular revela los hallazgos típicos de hipogonadismo hipogonadotrófico (3).

Nuestra paciente se nos presenta con los caracteres del síndrome casi en una forma completa. Presenta obesidad, retardación mental, estrabismo, coloboma del iris, sindactilia y polidactilia. En su familia no se presentan formas incompletas de la afección, pero cabe recalcar que ambas abuelas son primas hermanas. Este hecho tiende a favorecer la posibilidad de herencia autosómica recesiva en la paciente, de la misma forma en que ha sido informada la condición en la literatura.

## Resumen

El síndrome de Laurence-Moon-Biedl-Bardet puede presentarse de forma completa o parcial. Las manifestaciones características son obesidad, retardación men-

tal, polidactilia, sindactilia, retinitis pigmentosa e infantilismo sexual. La estatura puede ser variable. Se caracteriza por una herencia mendeliana autosómica recesiva.

Resumimos en esta comunicación las manifestaciones de los casos reportados en la literatura y las de un caso nuestro.

## Summary

Laurence-Moon-Biedl-Bardet syndrome manifests itself in a complete or partial forms. In the latter, the diagnosis is often difficult to make. In the complete form the cardinal features are obesity, mental retardation, polidactily and/or syndactily, retinitis pigmentosa and sexual infantilism. Short or normal stature may be present. Other associated anomalies have been described and are summarized in the text.

The condition is inherited by mendelian autosomal recessive inheritance. Over 300 cases have been reported in the world literature. The reported anomalies in the literature and the ones presented by our patient are summarized in the text.

## Agradecimiento

Al Dr. Arnaldo Muñoz Candelario por referirnos la paciente. A los Dres. C. Romaguera y E. Martin Ellis por la evaluación oftalmológica. A la Sra. Madeline Ruiz de Martínez la evaluación psicométrica de la paciente y a la Sra. Mirna Nazario por la excelente labor secretarial.

## Referencias

1. Laurence, J. Z., y Moon, R. C.: Four cases of "retinitis pigmentosa", occurring in the same family and accompanied by general imperfections of development. *Ophth. Rev.* 2: 32, 1865.
2. Smith, D. W.: Recognizable patterns of human malformation. W. B. Saunders Comp. Pg. 86-87, Filadelfia 1970.
3. Rosenthal, K.: Sexual infantilism, en *Endocrine and Genetic Diseases of Childhood*, editado por Lytt Gardner, W. B. Saunders Comp., Pg. 567, Filadelfia, 1969.
4. Wilkins, L.: Diagnóstico y tratamiento de las enfermedades endocrinas en la infancia y la adolescencia, Pg. 275 Editorial Espaxs, Barcelona, 1966.

5. Krill, A. E. y colabs.: Electroretinography in the Laurence-Moon-Biedl Syndrome. Am. J. Dis. Child. 102: 205, 1961.
6. Bell, J.: The Laurence-Moon Syndrome; en L. S. Penrose (Ed.): The treasury of human inheritance; London, Cambridge University Press, 1958, Vol. 5 Part 3.
7. Nelson, W. E. (editor) Textbook of Pediatrics, 10<sup>a</sup> edición-  
W. B. Saunders Comp., Filadelfia - 1975.
8. Bauman, M. y Hogan, C. R.: Laurence Moon Biedl Syndrome. Amer. J. Dis. Child. 126: 119-126, 1973.
9. Gellis, S. (editor). Year Book of Pediatrics 1975, Year Book Medical Publishers, Pg. 433.

# EVALUATION OF CELLULAR MEDIATED IMMUNITY IN A NORMAL ADULT POPULATION

Francisco Robert, MD  
José A. Lozada, MD  
Francisco J. Muñiz, MD

Impairment of cellular mediated immunity is frequently seen in patients with neoplastic diseases. This is more so in patients with markedly advanced and widely spread malignant tumors (1, 2). Whether this immune impairment is due to the etiologic agent of the tumor, the tumoral cells or whether it is actually one of the causes collaborating to tumor growth and development, remains to be established.

Further and more extensive evaluation of cellular immune response of patients with cancer may be of help in determining its role in tumor development and spread. Furthermore, a practical aspect of the elucidation of tumor and immune response relationship, would be its application in the early detection of malignancies, as well as in the establishment of a logical basis for the chemo-immunotherapy of cancer (3).

As a first step in our effort to evaluate the correlation of cellular immune response with malignancies in our Puerto Rican patients, we decided to determine (as a control for future studies) the cellular immune response in our normal (non-cancer) adult population. One of the methods used for establishing such data in normal subjects was skin testing of delayed hypersensitivity reaction to various antigens. In this communication we present the data obtained in 86 normal adults using skin tests with a chemical substance, Dinitrochlorobenzene (DNCB), and various bacterial viral and fungal (BVF) antigens such as mumps, candida, PPD and streptokinase antigens.

## Materials and Methods

1. Cutaneous reactivity to different antigens was determined in 86 normal adult volunteers with ages ranging from 12 to 96 years (Table I). These individuals showed no evidence of infectious or neoplastic disease, and had no history of receiving immunosuppressive drugs or diseases affecting immunocompetence. Both sexes were equally represented.

### 2. DNCB Contact Sensitization

The technique employed was the one previously described by Catalana et al (4). One thousand ug of DNCB were applied to the upper arm simultaneously with 100 ug of DNCB applied to the ipsilateral forearm. These doses were applied topically in areas previously cleaned with acetone and confined by a plastic ring 2.0 cm. in diameter. A spontaneous flare at both 1,000 ug and 100 ug sites by 14 days was scored as 4+ (fig. 1A and B). A spontaneous flare at the 1,000 ug site only was scored as 3+. If neither site developed a spontaneous flare by 14 days after application of DNCB, a challenge dose of 100 ug was applied. If spontaneous flare occurred at this site within 48-72 hours, it was scored as 2+. Occasionally, a questionable reaction was corroborated by skin biopsy and if the histologic features described below were present, it was scored as 1+. If no grossly visible reaction occurred, the subject was considered anergic to DNCB.

The biopsies were done using a standard skin punch-biopsy technique. Specimens were fixed in a formal solution and stained with hematoxylin and eosin. Lesions were scored as histologically positive if they showed lymphocytic and histiocytic infiltration at the dermal-epidermal junction and around the small vessels in the dermis (Fig. 2A, B and C).

### 3. Skin Test Antigens

The following commonly encountered antigens were employed in the skin tests.

- a. Purified Protein Derivative-intermediate strength (Con-nough).
- b. Candida Antigen (Dermatophytin "O" - undiluted Hollister-Stier).
- c. Streptokinase 20,000 ug - Streptodornase 5,000 u



TABLE I  
AGE RANGE DISTRIBUTION OF NORMAL ADULT SUBJECTS

AGE (Years)	Number of Subjects
12 - 20	1
21 - 30	24
31 - 40	17
41 - 50	8
51 - 60	5
61 - 70	15
71 - 80	13
81 - 90	2
91 - 100	1



Figure 1: An unequivocal positive reaction to D. N. C. B. skin test. In A there is evidence of spontaneous flare, manifested by marked erythema and induration. In B, a higher magnification of the above grossly changes are seen.

(Varidase, Lederle)  
d. Mumps Antigen (Lilly)

## Results

0.1 ml. of each antigen were injected intradermally and read at 48 hours. Interpretation of tests is described in Figure 3.

## Immune Response to DNCB

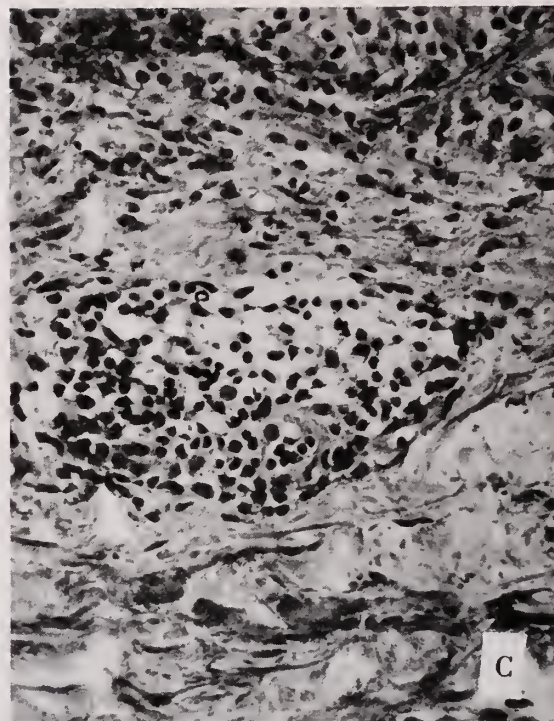


Figure 2: *Biopsies of D. N. C. B. Skin Test.* In A is shown a negative skin biopsy. In B a positive histology is shown; there is marked lymphocytic histiocytic infiltration at the dermal-epidermal junction. In C, a higher magnification of the biopsy shown in B, where the mononuclear cell infiltration around small vessel in the dermis is clearly shown.



Eighty seven percent (75/86) of normal subjects tested for delayed immune response with DNCB gave a response (spontaneous flare) in the area of antigen application to the skin (See Table II).

When subjects were divided into two age groups (those 50 years or younger and those 51 years or older) it was noted that 100 percent (50/50) of the subjects in the younger group were responsive to DNCB. On the other hand 71 percent (27/36) of the older subjects responded to DNCB. That is, eleven members (29 percent) of the older age group failed to recognize DNCB and to develop a delayed cellular immune reaction to it.

A further interesting observation is that all but two of the DNCB positive subjects gave a clear cut spontaneous skin flare reactions (2 + to 4 +). The two remaining subjects were shown to be positive by "punch type" skin biopsy. Although all non-responders belonged to the older age group, the intensity of the response (2 +, 3 + etc.), was in general of equal to that of the younger age group. Most subjects experienced mild to



TABLE II  
INCIDENCE OF REACTIVITY TO DNCB AND COMMON  
SKIN TEST ANTIGENS IN NORMAL VOLUNTEERS

Age	No. Volunteers	No.	DNCB		PPD	(+) SKIN TEST ANTIGENS (PERCENTAGES)		
			POS.	Neg.		Candida	Mumps	Streptok-Str Pt.
12-50	50	50	(100 %)	0	35 %	100 %	47 %	77 %
51-100	36	27	( 71 %)	11	38 %	88 %	30 %	73 %
All ages	86	75	( 87 %)	11	37 %	93 %	41 %	75 %

### Skin Tests Interpretation

#### Bacterial, Fungal and Viral Antigens

Tests are read at 48 hours after subcutaneous injection

Test was considered Positive when:

1. Mumps — 1.5 cms. or more of erythema with or without induration.
2. Candida — 0.5 cms. or more of induration.
3. PPD — 0.5 cms. or more of induration.
4. Streptokinase — 0.5 cms. or more of induration

Figure 3

moderate irritative reaction such as localized pruritus and burning sensation.

#### Immune Response to Bacterial, Viral & Fungal (BVF) Antigens

The incidence of reactivity to each of the BVF antigens is shown in Table II. It is worthwhile to note that Candida antigens skin testing yielded positive reactions in all fifty members of the younger group. Streptokinase — was positive in 39 of the fifty (39/50) members of the younger group (77 percent). Reactivity

to mumps and PPD antigens was 41 percent and 37 percent respectively. The incidence of reactivity to the above mentioned antigens in members of the older age group roughly paralleled the results obtained in the younger age group with 88 percent reactivity to Candida, 73 percent reactivity to Streptokinase, 38 percent reactivity to PPD and 30 percent reactivity to mumps. In members of the younger group, 25 percent were positive to three of the tests and 53 percent of the group (19 of 36) were positive to at least two tests. Six (17 percent) were positive to one test and one subject (2.5 percent) was negative to all of them.

Another interesting result, was that of the eleven non-reactors to DNC. All of them showed positive skin reactions to the bacterial-viral and fungal agents with the following distribution: Three (27 percent) of the eleven persons were positive to more than two antigens, four (36 percent) were positive for two antigens and four (36 percent) were positive for one antigen.

### Discussion

There is now evidence that some cells destined to serve immunologic functions arise from primitive pluripotent (Stem) cells located in the bone marrow. One of the most important type of cells responsible for the immunologic functions is the lymphocyte.



In accordance with the present concepts there are two types of lymphocytes: T and B lymphocytes. T-lymphocytes originate from the above mentioned stem cells. The T-lymphocytes develops under the influence of the thymus and engage in cell mediated immune functions, such as: graft rejection, protection against viruses and fungi and delayed skin hypersensitivity reactions (5). B-lymphocytes seem to develop independently from the thymus and eventually become antibody-producing cells. In birds, these B-cells are influenced by an intestinal organ called the "Bursa of Fabricius" however, in humans a bursa-equivalent organ has not been localized.

The use of skin testing with various chemical, bacterial, viral and fungal antigens is an established form of "in vivo" evaluation of the cellular immune response. This type of reaction is depressed by the administration of steroids, some anti-cancer drugs reticulo-endothelial malignancies and other type of disseminated malignancies.

Our initial experience with this mode of evaluation of immune response is the theme of this report. It is worthwhile to note that in persons 50 years or younger a 100 percent response was obtained with the chemical sensitization to DNCB and practically all of them responded to at least two antigens of the BVF group. The rate of skin reactivity to DNCB among the 50 years or older group was not as complete (71 percent) but the great majority of those who failed to respond to DNCB responded to two of the BVF antigens and all of them responded to at least one. It is our conclusion that the combination of DNCB testing and the four BVF antigen testing is an effective form of evaluation of cellular immune response.

There are "in vivo and in vitro" tests to assess the capacity of each of the components of the immune system. In our study only one type of "in vivo" evaluation of the T-cell System was determined. This evaluation is represented by the cutaneous-delayed hypersensitivity reactions to common BVF antigens and contact sensitization to a chemical agent. As a test for cellular immunity, DNCB contact sensitization offers several advantages over intradermal common antigens tests. Reliance upon previous exposure to the allergen is unnecessary since both sensitization and challenge are controlled and approximately 85-95 percent of normal people can be sensitized to this agent (4). However, contact sensitization to DNC offers several disadvantages, first it is a potent irritant and second, the development of sensitization

requires 7 to 21 days.

The incidence of reactivity to DNCB and common skin test antigens in our normal adult population is somewhat similar to that presented by Young et al (6) using North Americans control patients. However, he reported a higher incidence of reactivity to DNCB (95 percent) and to Mumps (88 percent) and lower incidence to candida (52 percent). One explanation for this difference in incidence of reactivity to BVF antigens could be a geographical variation of common antigen (bacterial, fungi) prevalence. All these findings emphasize the importance of doing a battery of multiple skin tests as part of a complete immunologic evaluation.

The concept of immunological surveillance proposed by Thomas and Burnet suggest that the growth of neoplasms may reflect a failure of cell-mediated immunity. Evidence supporting this hypothesis is the observation that in man and in many animal models, cancer incidence is highest at the extremes of age, especially in the older population. This relationship was clearly shown by Dorn et al (8). When he published an statistical data of morbidity from cancer in the United States. He found that the occurrence of cancer increases with age from an incidence of 13/100,000 persons at age 15 yr. to 3,000/100,000 persons at age 90. Probably one explanation of the high incidence of cancer at this age is that cellular immune responses might decline with age. Weksler (9) showed that lymphocytes from old persons have a decreased response to plant mitogens and allogeneic lymphocytes when compared with lymphocytes from young persons. He postulated that this altered reactivity of thymus-derived lymphocytes in aged subjects cannot be attributed to a deficiency of T-cells; his study demonstrated that the number of these cells is maintained in old persons (9). It has been found recently that the concentration of thymosin in the blood declines with age (10). All these observations support the hypothesis of a qualitative dysfunction of the thymus-derived lymphocyte system in older subjects.

Our results show that the incidence of sensitization to DNCB was lower in the aged population (Table II). Waldorf, Willkens and Decker (11) found a similar low incidence of reactivity to DNCB in aged persons. An observation that is particularly relevant in our study, is the correlation between the incidence of reactivity to DNCB and common skin test antigens in both groups of volunteers. Although the aged persons were less reactive to DNCB this difference

in reactivity was not observed with the other common antigens. A high incidence of reactivity to two or more common antigens was also found in this group of old persons, including those subjects anergic to DNCB. Probably, the qualitative dysfunction of the T-cell System become more impaired in the process of sensitization to new antigens such as DNCB. This defect may be an abnormality in the recognition or processing of new antigens or in the proper transfer of the immune message to the effector cells.

Whatever the explanation for the immunological impairment in cancer patients, it is apparent that its presence indicates a poor prognosis for these patients (12). Immunologic studies are therefore useful prognostic tests in the evaluation of the patient with cancer.

This evaluation of cellular immunity in a Puerto Rican adult population can serve as a reference point in the immunologic evaluation of cancer patients in our Island.

## References

1. *Al-Sarraf, M., et al.*: Clinical Immunologic Responsiveness in Malignant Disease. *Cancer* 26: 262-267, 1970.
2. *Anthony, H. M., et al.*: The prognostic significance of DHS Skin Tests in Patients with Carcinoma of Bronchus. *Cancer* 34: 1901-1906, 1974.
3. *Twomey, P. L., Catalona, W. J., Chrentien, P. B.*: Cellular Immunity in Cured Cancer Patients. *Cancer*, 33: 435-440, 1974.
4. *Catalona, W. J., Taylor, P. T., Rabson, A. S.*: Sensitization: A Clinicopathological Study. *New England J. of Med.* 286: 399-402, 1972.
5. *Daguillard, F.*: Immunologic Significance of in vitro Lymphocyte Responses "In" The Medical Clinics of North America 56: 293-299, 1972, Saunder Company.
6. *Young, R. C., Corder, M. P., De Vita, V.*: Immune Alterations in Hodgkin's Disease *Arch of Int. Med.* 131: 446-454, 1973.
7. *Waldmann, T. A., Strober, W., Blaese, M.*: Immunodeficiency Disease and Malignancy. *Ann. of Int. Med.* 77: 605-628, 1972.
8. *Dorn, H. F., Cutler, S. J.*: Morbidity from Cancer in the United States, Public Health Monogr. N. 56, 1959.
9. *Weksler, M. E., Hüterroth, T.*: Impaired Lymphocyte Function in Aged Humans. *J. Clin. Invs.* 53: 99-103, 1974.
10. *Schulof, R. S., Hooper, J. A. White, A., Goldstein, A. L.*: Development of radioimmunoassays for human and bone thymosin. *Fed. Proc.* 32: 962, 1973. (Abstr.)
11. *Waldorf, D. S., Willkens, R. F., Decker, J.*: Impaired delayed hypersensitivity in an aging population. *J. Am. Med. Assoc.* 203: 111, 1968.
12. *Morton et al.*: Immunological Aspects of Neoplasia. *Ann. of Int. Med.* 74-587, 1971.

## INFLUENZA – TREATMENT AND PREVENTION

Carlos F. León-Valiente, MD

Carlos H. Ramírez-Ronda, MD, FACP

Ramón H. Bermúdez, MD

Influenza is a viral disease characterized by a sudden episode of fever, chills, headache, dry cough, soreness and aching in the back and limbs. Fever seldom lasts more than several days, although the patient may continue to feel weakness for several days to a week or more.

The etiologic agents in influenza are the influenza viruses, types A, B & C and their variants. The infection with one type confers no immunity to infection with the other two. Influenza viruses are of the myxovirus group and related to mumps, measles, and parainfluenza viruses: are composed of a helicoidribonucleid-protein core covered with coat proteins of two types, hemagglutinins (H) and neuramidase (N). Both substances are antigenic and elicit protective antibody. Antigenic shifts in influenza viruses are due to changes in the coat proteins. The designation of antigenic changes and the major occurrence of influenza for which they were responsible are:

- a. Pandemic 1918: Swine-flu agent.
- b. Epidemic 1933:  $H_2N_1$ , formerly  $A_0$ .
- c. Epidemic 1947:  $H_1N_1$ , formerly  $A_1$ .
- d. Pandemic 1957:  $H_2N_2$ , formerly  $A_2$  or Asian.
- e. Pandemic 1968:  $H_3N_2$ , or Hong Kong.

Influenza A is responsible for large epidemics and pandemics associated with complications and an increased mortality. The 1918 pandemic resulted in a worldwide death toll of 20 million. Changes in the antigenic determinants will determine the severity of the illness.

*From the Infectious Disease Section, Departments of Medicine and Research, Veterans Administration Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.*

*For reprints write to: Carlos H. Ramírez Ronda, MD, Infectious Diseases Section, VA Hospital, GPO Box 4867, San Juan, Puerto Rico 00936.*

Influenza B, in contrast to influenza A, is responsible for small epidemic outbreaks associated with high morbidity and low mortality. Influenza B has also been reported to be associated with Reye's syndrome.

In February 1976, a new strain of human influenza virus, designated A, New Jersey-76, was isolated during an outbreak of respiratory disease among Army recruits at Fort Dix, New Jersey. This outbreak was the first known example in the U. S. since 1930 of person to person transmission of swine influenza virus. It is this swine influenza A virus the one that possibly will be responsible for next expected epidemic. A pandemic is expected since the majority of persons do not presently have specific antibodies and are susceptible.

Clinically, influenza is a disease with very little specific signs and symptoms. It is manifested by general malaise, headache, fever, loss of appetite, eyes pain, myalgias, dry cough, sore throat, hoarseness, diffuse chest pain and coryza in the majority of cases. The diagnosis is made clinically, serologically and by viral cultures. The serologic studies available are the complement fixation test and/or the hemagglutination inhibition antibody test. Serologic diagnosis is based on a four-fold rise in titer performed with acute and convalescent serum usually taken two weeks apart. The diagnosis is also made by the isolation of the virus on chick embryo cultures. In the early stages of disease, you find lymphocytosis with or without neutropenia, and later, specially if secondary bacterial infection of the respiratory tract occurs, there is leukocytosis with shift to the left.

Even though some authors believe that the virulence of influenza A swine has not changed in the last 50 years, we must be prepared for a change in virulence since antibody protection for the new virus strain is low or none. We know that the mortality is variable, highest during pandemics and epidemics as the result of higher complication rates.

The mortality in influenza is secondary to its com-



plications. The majority of complications usually occurs in patients with underlying disease. Patients with cardiovascular disease, pulmonary disease, diabetes mellitus, liver cirrhosis and pregnant women, have a greater tendency to develop complications. This group of patients is the one to receive prophylaxis and vaccine always.

Complications in influenza can be divided into respiratory and non-respiratory complications. Non-respiratory complications include cardiac complications such as myocarditis and pericarditis. It is important to remember that in patients taking digoxin because of heart failure, when they develop influenza, the serum digoxin levels have a tendency to decrease and cause the clinical picture of intractable failure. Some neurological complications have also been found. These include encephalitis, appearing 2-3 days after the onset of influenza, and only requiring supportive therapy and Guillain Barré Syndrome that requires prompt supportive treatment to prevent further complications. There is an increase in the mortality of pregnant women who have influenza, specially during the second half of pregnancy. There has been no correlation between premature births or fetal deaths and influenza epidemics, although variable congenital defects have been reported in approximately 3 percent of newborns.

Of the respiratory complications, the most important ones are those involving the lower respiratory tract. In this respect, although bronchitis and bronchiolitis can be found, pneumonias are the most important.

Pneumonia occurring in influenza can be separated into primary viral pneumonia, early bacterial pneumonia and late bacterial pneumonia. In late bacterial pneumonia, one may find reports of 15-69 percent of cases caused by *Streptococcus pneumoniae*, while other authors found that 60 percent of the cases were caused by *Staphylococcus aureus*.

Clinically, late bacterial pneumonia following influenza is characterized by the picture of influenza that is followed by clinical improvement of one to four days. After improvement the patient develops new fever, chills, pleuritic chest pain and bloody sputum. On physical examination one finds a focal lung consolidation; sputum gram stain and culture usually are positive. The treatment is with antibiotics against the specific bacteria. Mortality is low.

Influenza viral pneumonia is characterized by symptoms of short duration manifested by severe shortness of breath and the development of clinical pneumonia usually occurring in less than 24-36 hours after

the patient is admitted to the hospital. On physical examination you can find diffuse and bilateral inspiratory rales, expiratory wheezes, cyanosis and respiratory distress. The blood count may be normal or elevated, the sputum culture and smear are negative, and the chest x-rays show a diffuse fanning, bilateral perihilar infiltrates, suggesting cardiac failure. This entity does not respond to antimicrobial therapy and the patient continues with hypoxia, respiratory distress and acidosis.

Another form of pneumonia is the combination of influenza pneumonia and bacterial pneumonia. It may present features of severe diffuse and focal bacterial infiltrates. Sputum culture may show pneumococcus, *Staphylococcus aureus*, *Hemophilus influenza* or viruses. This combination is associated with a significant mortality.

Although the view has been widely held that influenza virus infection per se does not produce fatal disease, it has long been recognized that influenza epidemics are closely associated with an increased incidence of bacterial pneumonia. Initially, in the post pandemic periods, *Hemophilus influenza* was isolated. Lately, in the majority of fatal cases, the associated bacterial pathogen has been *Staphylococcus aureus*, specially in association with influenza virus infection. The picture of staphylococcus as an increasingly co-invader in influenza must be reviewed with caution. There have been recent reports of a high incidence of pneumococcal pneumonia which is contrasted with a low incidence of pneumococcus reported in autopsy material from fatal cases of influenza. The wide use of antimicrobial agents, may thus, in part, select the bacterial agent, staphylococcus, which will result in an influenza fatality.

The management of the influenza patient with pneumonia should be aggressive and prompt. The sputum, if available, and identified as true sputum and not saliva, can be used for identification of the organism with a gram stain. If there is not a good specimen, a transtracheal aspiration should be performed in this patient with a potential lethal condition and a gram stain of the transtracheal aspirate will dictate therapy. If gram positive cocci in clusters are found, specific antibiotic therapy with methicillin, nafcillin or penicillin should be started.

### Chemotherapy of Influenza

During many years the virologists have kept some

hope in the development of antiviral agents, and specifically, against the influenza virus. Some years ago this optimism increased with the discovery of interferon, by Isaac and Lindermann, as well as with the effect of amantadine hydrochloride in the influenza virus.

Of all the agents, only amantadine hydrochloride was proven to have some effect in the control of influenza in adults. It has been shown to be effective in the treatment of influenza A and B, specifically A<sub>2</sub>. Amantadine hydrochloride is a synthetic salt derived from a primary amine, studied in the decades of 1960 against influenza A virus and its variants. It is absorbed and excreted without being metabolized and accepted serum levels are obtained between twenty to forty hours of the ingestion, reaching an equilibrium with a single daily dose. To be effective it has to be circulating in the body before the patient gets in contact with the virus. It does not have any antipyretic, antihistaminic nor analgesic effect. Its effect is directly against the virus. It is believed that amantadine blocks the viral penetration at the cell membrane, decreasing its absorption. Possibly, it may inhibit the enzymes that facilitate the cell penetration or it may block only the access to the cell membrane where the virus penetrates. The drug has to be given, at least, 24 to 36 hours prior to being exposed to the virus, to have a prophylactic effect. It has been found that if the drug is given once the patient has developed the symptoms, the duration of symptoms may decrease by 50 percent. The optimal dosage in adults of amantadine is between 200-300 mg per day. No significant toxicity has been documented at this dosage. If the dosage is increased, some patients may present an amphetaminic effect manifested by anxiety, hallucinations, blurred vision, bradycardia and a decrease in the urinary output. With amantadine we have a drug that is effective against influenza in adults if it is used correctly, but never should be considered as an alternate to the vaccine. The drug should be used in all patients who represent a high risk and in all patients who may be exposed to influenza virus, patients with diabetic, cardiac, chronic lung conditions, and old persons. At the first evidence that influenza is present in an unvaccinated community, these patients should receive the dosage previously mentioned and should receive it for a 3 to 4 month period. Although the FDA has not approved the use of amantadine in patients who already have influenza, many authors recommend its use if it is given during the first 24 to 36 hours after the onset of symptoms. The limi-

tation on use is cost.

Another preparation that has, at one time or another, been suggested as a possible antiinfluenza agent is interferon. It is a natural product of virus infected leukocytes with a broad-range of nonspecific antiviral activity. It is of great scientific interest but so far is of no practical clinical value. It is possible to induce interferon production experimentally in animals and man, but we have not yet found a safe and reliable means of using the process for the protection of man against viral infections. Exogenous interferon produced by treating human leukocytes in vitro, has been reported to reduce the incidence of A-2 influenza by 50-60 percent. The significance of the results is not clear and it was concluded that the degree of protection may also have varied with the individual's ability to elaborate interferon and with the innate capacity of the influenza virus to elicit an endogenous interferon response. It is concluded at the present time, that interferon does not have any clinical application against influenza.

### Active Immunization

The most effective way we have at present of prophylaxis against influenza is by means of active immunization.

The vaccine is obtained using the viruses and its antigenic variants, inactivated by formalin or attenuated by successive culture passages. It is very important to maintain the antigenicity in order to obtain high antibody levels in serum. The major problem is the manufacture of the vaccine lies on the antigen changes that occur to the virus every eight to ten years. It is known that the vaccine used correctly and including the specific viruses can reduce the incidence of influenza in 75-80 percent of the cases. The present highly purified vaccines are given intramuscularly and produce very few side effects.

An experimental mode of administration of live-virus influenza vaccine is by the intranasal route. Even though proven effectively in some cases, its wide spread use has not been accepted and its use is still under investigation.

The use of the parenteral influenza vaccine is indicated in every adult patient who represents a high risk: diabetics, patients with heart, kidney or lung disease, patients with hypertension, the elderly, the debilitated and those persons that may be exposed

to the virus. It is very important that vaccination occurs 4-6 weeks prior to exposure to the virus so that the patient have enough time to develop antibodies. Children with underlying disease should receive two doses of split virus vaccine at least four weeks apart. The side effects are few. The vaccine is contraindicated in people allergic to eggs. We encourage to have everyone vaccinated for the forthcoming influenza epidemic.

### References

1. Cluff, L. E.: Influenza. In L. E. Cluff and J. E. Johnson (ed) Clinical Concepts of Infectious Diseases. The Williams & Wilkins Co., Baltimore, 1972, p 152-159.
2. Fox, J. P., Kilbourne, E. D.: Epidemiology of influenza. Summary of influenza workshop IV. J Infect Dis 128: 361-386, 1973.
3. Harris, C. S. : Influenza vaccines. Ann Intern Med 80: 469, 1974.
4. Pérez, F., Bermúdez, R. H., Brau, C. J., et al: Attenuated influenza virus intranasal vaccine in a high risk male population. Bol Asoc Med P R 67: 376, 1975.
5. Rubén, F. L., Akers, L. W., Stanley, E. D. and Jackson, G. F.: Protection with split and whole virus vaccines against influenza. Arch Intern Med 132: 568, 1973.
6. Sanford, J. P.: Influenza: Consideration of pandemics. In G. H. Stollerman (ed), Advances in Internal Medicine, Vol 15, Year Book Medical Publishers, Chicago, 1969, p 519-453.



## WATER CONTACT PATTERNS AND BILHARZIASIS

---

*Bilharziasis (schistosomiasis) in Puerto Rico is a man to snail to man infection since there are no important reservoir hosts on our island. Surveys for bilharziasis in Puerto Rico held over the past 30 years clearly demonstrate a small but definite decrease in infection rates. Prevalence rates have decreased to less than 10 percent, although some rural communities show rates as high as 40 percent. There has also been a definite decrease in clinical bilharziasis, for example the hepatosplenic form, which may have required portacaval shunts.*

*However, acute bilharziasis has been increasing in Puerto Rico. Outbreaks of this form have been detected repeatedly since 1965. Furthermore, over the past 10 years we have observed increases in country homes for recreation by the more affluent. We have also observed increases in camping and picnics by families near our freshwater streams and lakes. Coupled with this, we now find increases in water contact for recreation by Puerto Rican families.*

*In an article published in this issue of the Boletín Lipes and Hiatt used a standardized questionnaire in a survey of 772 individuals from 3 urban San Juan neighborhoods to determine the frequency and characteristics of water contact practices as potential risk factors in the transmission of bilharziasis. Their results include the following: (1) twenty-three percent of the individuals surveyed admitted that they had come in contact with freshwater streams of Puerto Rico; (2) the family was the most important social unit associated with water contact; (3) the majority of the water contact was by persons under 30 years of age and those with most frequent water contact under 20 years of age thus paralleling the peak prevalence of infection on the island; (4) water contact was most frequent during the summer months at a time when there is an increased risk of infection because of higher water temperatures and more sunlight which favor the proliferation of the snail intermediate host and emergence of infective cercariae; (5) the nature of the water contact was principally swimming; (6) the proportion of people admitting to water contact decreased as their level of knowledge of bilharziasis increased; and (7) a good number of the sites where water contact occurred are in the areas most endemic for bilharziasis.*

*These studies by Drs. Lipes and Hiatt point out a simple approach to obtain information on water contact patterns of humans who may be exposed to bilharziasis. They may also help formulate, on a rational basis, the most useful public health education and control measures to eradicate this parasite from the island.*

*George V. Hillyer, Ph.D.*

$\frac{20}{150}$

# H

$\frac{20}{100}$

# E A R

$\frac{20}{70}$

# I N G I S

$\frac{20}{50}$

# A S P R E C I O U S

$\frac{20}{40}$

# A S S I G H T H A V E

$\frac{20}{30}$

# Y O U H A D Y O U R H E A R I N G

$\frac{20}{20}$

# T E S T E D L A T E L Y A S I M P L Y

$\frac{20}{15}$

# C O M F O R T A B L E H E A R I N G

$\frac{20}{10}$

# I N V E S T M E N T O F A F E W M I N U T E S

Hearing losses are among the most consistently neglected health problems. Many people with them won't even admit it to themselves, let alone others. A little encouragement may start them thinking about themselves more realistically.

That's why we're offering you the poster shown here. You can hang it on the wall or stand it on a small table. It comes with booklets called "As precious as sight" that give your patients some basic facts about auditory testing and hearing losses and how easy they are to correct in many cases.

Write to us for your free poster and booklets. They just might help you to help some patients who aren't hearing as well as they used to. Even those who ordinarily wouldn't hear of it.

Professional Relations Division, Beltone Electronics Corporation  
4201 West Victoria Street, Chicago, Illinois 60646, an American company

***Beltone***  
WHEN A HEARING  
AID WILL HELP



Lector



# When choosing a diuretic for day-in-day-out hypertension control with comfortable compliance...

The agent you choose in mild to moderate essential hypertension should offer (1) long-term effectiveness, (2) patient comfort and compliance.

## Zaroxolyn offers both.

In one long-term study<sup>1</sup> Zaroxolyn brought moderately elevated (average 161/109 mm Hg) blood pressure down to the range of normotension—and held it there for a year or more.

The investigator noted, "Patient cooperation was surprisingly good for a study of such duration [2½ years]. The once-daily dosage schedule with

metolazone [Zaroxolyn] no doubt contributed to patient compliance."

Overall compliance with Zaroxolyn is good—very good. An analysis of controlled clinical studies involving 188 Zaroxolyn patients showed that only eight discontinued therapy because of side effects. That's a discontinuation rate of only 4.3%, and broader clinical experience appears to substantiate this low rate?

Zaroxolyn. For long-term control and comfortable compliance in mild to moderate hypertension.

Recommended initial dosage in mild to moderate essential hypertension—2½ to 5 mg once daily

# Zaroxolyn<sup>®</sup>

(metolazone, Pennwalt)

2½-mg, 5-mg and 10-mg tablets

## once-daily antihypertensive diuretic


Before prescribing, see complete prescribing information in the package insert, or in PDR, or available from your Pennwalt representative. The following is a brief summary. **Indications:** Zaroxolyn (metolazone) is an antihypertensive diuretic indicated for the management of mild to moderate essential hypertension as sole therapeutic agent and in the more severe forms of hypertension in conjunction with other antihypertensive agents. Also, edema associated with heart failure and renal disease. **Contraindications:** Anuria, hepatic coma or precoma; allergy or sensitivity to Zaroxolyn. Or, as a routine in otherwise healthy pregnant women. **Warnings:** In theory cross-allergy may occur in patients allergic to sulfonamide-derived drugs, thiazides or quinethazone. Hypokalemia may occur, and is a particular hazard in digitalized patients; dangerous or fatal arrhythmias may occur. Hyponatremia and hyperuricemia may be noted or precipitated. Considerable potentiation may occur when given concurrently with furosemide. When used concurrently with other antihypertensives, the dosage of the other agents should be reduced. Use with potassium-sparing diuretics may cause potassium retention and hyperkalemia. Administration to women of childbearing

age requires that potential benefits be weighed against possible hazards to the fetus. Zaroxolyn appears in the breast milk. Not for pediatric use. **Precautions:** Perform periodic examination of serum electrolytes, BUN, uric acid, and glucose. Observe patients for signs of fluid or electrolyte imbalance. These determinations are particularly important when there is excessive vomiting or diarrhea, or when parenteral fluids are administered. Patients treated with diuretics or corticosteroids are susceptible to potassium depletion. Caution should be observed when administering to patients with gout or hyperuricemia or those with severely impaired renal function. Hyperglycemia and glycosuria may occur in latent diabetes. Chloride deficit and hypochloremic alkalosis may occur. Orthostatic hypotension may occur. Dilutional hyponatremia may occur in edematous patients in hot weather. **Adverse Reactions:** Constipation, nausea, vomiting, anorexia, diarrhea, bloating, epigastric distress, intrahepatic cholestatic jaundice, hepatitis, syncope, dizziness, drowsiness, vertigo, headache, orthostatic hypotension, excessive volume depletion, hemoconcentration, venous thrombosis, palpitation, chest pain, leukopenia, urticaria, other skin rashes, dryness of mouth,

hypokalemia, hyponatremia, hypochloremia, hypochloremic alkalosis, hyperuricemia, hyperglycemia, glycosuria, raised BUN or creatinine, fatigue, muscle cramps or spasm, weakness, restlessness, chills, and acute gouty attacks. **Usual Initial Once-Daily Dosages:** mild to moderate essential hypertension—2½ to 5 mg; edema of cardiac failure—5 to 10 mg; edema of renal disease—5 to 20 mg. Dosage adjustment may be necessary during the course of therapy. **How Supplied:** Tablets, 2½, 5 and 10 mg

### References:

1. Dornfeld L, Kane R: Metolazone in essential hypertension. The long-term clinical efficacy of a new diuretic. *Curr Ther Res* 18: 527-533, 1975
2. Data on file, Medical Department, Pennwalt Prescription Products.

 **PENNWALT**  
Pennwalt Prescription Products  
Pharmaceutical Division  
Pennwalt Corporation  
Rochester, New York 14603

# DYAZIDE®

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

Trademark

## MAKES SENSE FOR LONG-TERM CONTROL OF HYPERTENSION\*



**LOWERS BLOOD PRESSURE**

**CONSERVES POTASSIUM**

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### \* WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

\* **Indications:** When the fixed combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome, corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium-sparing action of its 'Dyrenium' component is warranted.

**Contraindications:** Further use in progressive renal or hepatic dysfunction; hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs. Routine use of diuretics in otherwise healthy pregnancy.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with

cardiac irregularities. It is more likely in severely ill patients with urine volume less than one liter/day, the elderly or diabetics, with suspected or confirmed renal insufficiency. Periodic determinations of serum K<sup>+</sup> should be made. If hyperkalemia develops, substitute a thiazide alone, restrict K<sup>+</sup> intake. The presence of a widened QRS complex or arrhythmia in association with hyperkalemia requires prompt additional therapy. Thiazides are reported to cross the placental barrier and appear in breast milk; fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and other adverse reactions that have occurred in the adult may result. When used in pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics, or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spiro-lactone is used concomitantly, determine serum K<sup>+</sup> frequently; both can cause K<sup>+</sup> retention and elevated serum K<sup>+</sup>. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium® (triamterene, SK&F Co.), and

leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Do periodic blood studies in cirrhotics to check for nondrug-related variations in blood pictures, and in patients with folic acid depletion, since 'Dyrenium' may contribute to appearance of megaloblastosis. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

**Adverse Reactions:** Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting; diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely allergic pneumonitis have occurred with thiazides alone.

**Supplied:** Bottles of 100 and 1000 capsules Single Unit Packages of 100 (intended for institutional use only).

**SK&F CO.,** Carolina, P.R. 00630  
Subsidiary of SmithKline Corporation

## TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE



## CONGRESOS TECNICOS INTERNACIONALES QUE SE REALIZAN EN FRANCIA

### JORNADAS DE INFORMACION MEDICA - TOULOUSE 22-25 DE MARZO DE 1977

Organizadas por el Instituto de Investigación de Informática y de Automatismo - IRIA, con la cooperación del Ministerio francés de Salud Pública, de la Asociación para las Aplicaciones de la Informática a la Medicina - AIM, de la Dirección de Investigaciones y de Medio de Ensayo - DRME y de la Sociedad de Electricistas, Electronicistas y Radioelectricistas - S.E.E. - se llevarán a cabo las Jornadas de Informática Médica en Tolosa, del 22 al 25 de marzo de 1977.

Se asegurará una traducción simultánea en los idiomas inglés y francés.

Informes: Institut de Recherche d'Informatique et d'Automatique - IRIA, Secrétariat des Journées, Service des Relations Extérieures, Domaine de Voluceau, Rocquencourt, 78150 Le Chesnay - France.

## AMA NEWS RELEASE:

### PHYSICIANS GET GUIDELINES ON HIGH BLOOD PRESSURE

CHICAGO— A useful guide to physicians on how to manage high blood pressure in their patients is offered in the Jan. 17 Journal of the American Medical Association.

The guide is a report of the Joint National Committee on Detection, Evaluation and Treatment of High Blood Pressure, a cooperative study involving nine national associations and government units concerned with the on-going nationwide campaign against high blood pressure.

The committee was formed by the National Heart, Lung, and Blood Institute, Bethesda, Md. Chairman is Marvin Moser, M. D., of White Plains, N. Y., senior medical consultant to the National High Blood Pressure Education Program.

The report gives six general recommendations to physicians for the detection, evaluation and treatment of high blood pressure in adults:

1. Any group measuring blood pressure should have resources available for referral, confirmation, and follow-up.
2. Virtually all patients with a diastolic pressure of 105 or

greater should be treated with anti-hypertensive drug therapy.

3. For persons with diastolic pressures of 90 to 104, treatment should be individualized, with consideration given to other risk factors.
4. The evaluation of patients with high pressure can be limited to a few baseline tests in most instances.
5. A stepped-care approach is advocated as a cost-effective method of treating most patients. Stepped care means the beginning of therapy with a small dose of a drug, increasing the dose of that drug, and then adding, one after another, other drugs as needed.
6. Treatment includes plans for facilitating long-term maintenance of blood pressure control.

"Management of high blood pressure must be considered a lifelong endeavor," the report says.

Most patients with uncomplicated high blood pressure have few, if any, symptoms related to their pressure; however, drug therapy may produce unwanted effects about which patients should be forewarned, the committee points out.

In an accompanying editorial, JAMA Editor William R. Barclay, M. D., points out to physicians that the guidelines in the report are useful in general terms, but should not be considered a rigid directive, and that treatment must be tailored to the individual patient.

### SURFBOARDING RANKED AS RELATIVELY SAFE SPORT

Risk of injury requiring hospitalization while surfboarding is approximately one in 17,500 surfing days, says Robert H. Allen, M. D., of the University of Hawaii Medical School, and colleagues. Skiers suffer up to one injury for every 100 snow-skier days, Dr. Allen points out.

Thirty-five surfing injuries required hospitalization at the Waikiki Kaiser Foundation Hospital between 1969 and 1975. Risk of injury is much less for surfboarding than for body-surfing, he found. There is risk of head and spine injuries while body surfing, and risk of being hit by a loose surfboard while surfboarding.

The Honolulu doctors compiled a list of safety measures for surfers to help minimize injuries.

For board surfers: (1) Study the surf, the bottom (rocks, coral, sand), the tides, and the traffic. Avoid reefs. Do not



take a wave that is too steep. Know your limit. Stay with your board, (2) Surf with a companion, but avoid waves already crowded with others. (3) When paddling out, avoid the path of surfers coming in. If an incoming board is on collision course, dive deep and stay down long. (4) If you fall, try to tumble behind the board — not in front. Try to turn the fall into a dive, going deep, and stay under a long time. Protect your head with your arms as you come up. (5) Where the water is shallow, fall flat, buttocks or feet first.

For body surfers: (1) Avoid areas where there are surfboarders, crowds of swimmers, protruding reefs or rip currents. (2) Stop when you get tired or have cramps. (3) To avoid hitting your head in the sand, arch your body with the head back when riding down the wave, and when exiting a wave roll to one side. (4) Surf where the waves break in water as deep as possible. Avoid shorebreaks.

and workshops. Topics will include:

- Problem-solving skills that can be applied to specific needs.
- Managerial duties related to physician privileges, rights, and responsibilities.
- Joint Committee on Accreditation of Hospitals accreditation standards applicable to the medical staff.
- Legal aspects of medical staff rights and responsibilities.
- Negotiation techniques.
- Risk management and medical liability problems.
- Professional liability insurance.

Additional workshops will be held June 10-11 in Atlanta; Sept. 16-17 in Columbus, Ohio; Sept. 23-24 in Philadelphia; Oct. 7-8 in Chicago, and Nov. 4-5 in Dallas.

Registration is limited. To receive further information, contact the Department of Hospitals and Health Facilities, AMA, 535 North Dearborn Street, Chicago, Illinois 60610.

---

#### AMA SCHEDULES WORKSHOPS FOR HOSPITAL MEDICAL STAFFS

CHICAGO— The American Medical Association will conduct a series of six regional workshops for hospital medical staff leaders of the present and future during 1977.

The first workshop will be held April 22-23 in San Francisco (Fairmont Hotel).

The two-day meetings have been designed to help medical staff leaders learn managerial skills needed to carry out the increasing responsibilities they face in developing bylaws, rules, and regulations; cooperating with other hospital groups to improve patient care; evaluating quality of medical care; and resolving conflicts that may arise between the hospital medical staff and the board of trustees and administration or within the medical staff itself.

The programs will consist of both general sessions group

---

#### DR. TAUSSIG TO RECEIVE AMA ACHIEVEMENT AWARD

CHICAGO— Helen B. Taussig, M. D., who helped develop the "blue baby" operation in the 1940s, will receive the American Medical Association's Scientific Achievement Award.

The award will be presented to Dr. Taussig at the AMA's annual convention in San Francisco on June 19, the AMA Board of Trustees announced.

Dr. Taussig, 78, is best known for recognizing and suggesting surgical correction of the "blue baby" syndrome to Alfred Blalock, M. D., the surgeon who first performed the operation.

She has also done extensive research in congenital heart disorders, and in the efficacy of surgery to correct such disorders. She was one of the first to publicize the potential harm to unborn children by Thalidomide, and to study the effects of drugs on unborn children.

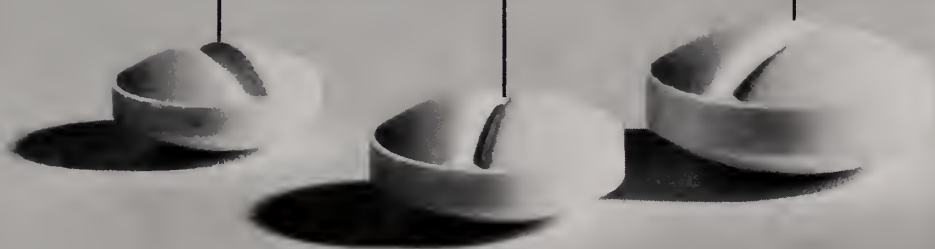
#### WANTED

Family practitioner and/or internist-cardiologist by six men multi-specialty group in Mid-East Tennessee. Town of 7,000 with a drawing area of 60,000 population. Modern Clinic Building adjacent to ultra-modern 200 bed Medical Center. No investment. First year guaranteed ample salary plus multiple fringe benefits. Must be able to obtain a Tennessee Medical License and speak English fluently. Ideal situation for a U. S. or P. R. trained physician wishing to relocate in U. S. If interested, contact: Ramón Sánchez Viñas, M. D., Cumberland Clinic, 301 Hayes Street, Crossville, Tennessee, 38555, (615) 484-5171.

100 mg

250 mg

500 mg



# **Tolinase<sup>®</sup>** **tolazamide, Upjohn**

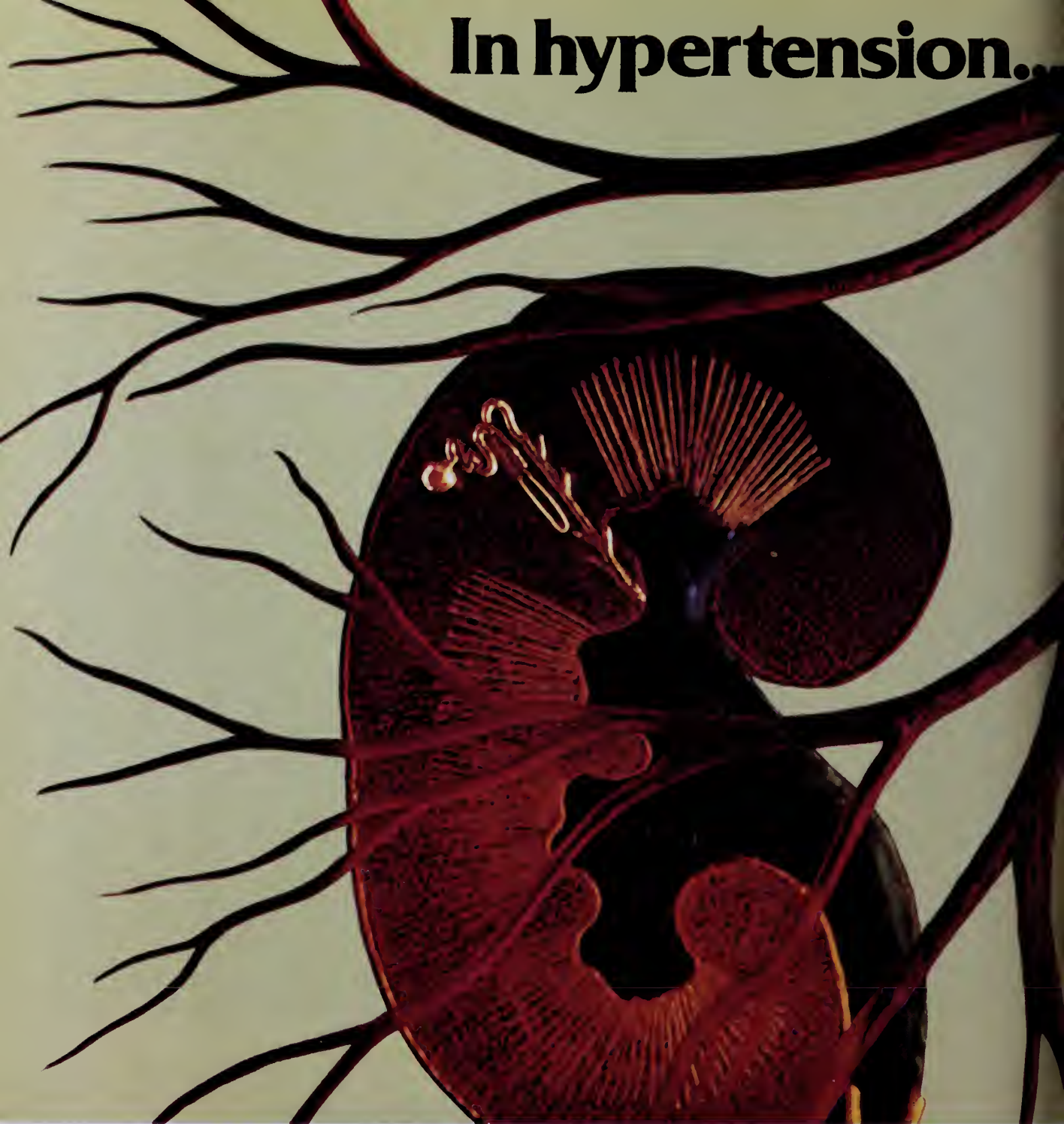
Please contact your Upjohn representative for additional product information.

**Upjohn**

J-5695-6

© 1977 THE UPJOHN COMPANY

# In hypertension..



## Brief Summary

**Indication:** Hypertension. (See box warning.) **Contraindications:** Mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.

## Warnings:

This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Use with caution in patients with severe renal disease, impaired hepatic function or progressive liver disease. Regroton may potentiate action of other antihypertensive, ganglionic and peripheral adren-

ergic-blocking drugs. Sensitivity reactions may occur in allergic and asthmatic patients. Discontinue Regroton one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Thiazides cross the placental barrier and appear in cord blood. The use of chlorthalidone and related drugs in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Use with care in nursing mothers since thiazides and reserpine cross the placental barrier and appear in cord blood and breast milk. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated mothers. If use of the drug is essential, the patient should stop nursing. **Precautions:** Antihypertensive therapy with this drug should always be initiated cautiously in post-

sympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use anticholinergic or adrenergic drugs or other supportive measures if needed. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue Regroton if the BUN rises or liver dysfunction is aggravated (hepatic coma may be precipitated). Patients receiving chlorthalidone should have periodic determination of serum electrolytes and should be observed for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis and hypokalemia), particularly if they are receiving digitalis, parenteral fluids, or are vomiting excessively. Hypokalemia may develop with chlorthalidone as with any other potent





# Regroton<sup>®</sup> (chlorthalidone/reserpine) for the paired problems of volume/vasoconstriction

## Multisite action

Through sodium excretion, volume reduction, decreased peripheral resistance and renin suppression, Regroton effectively reduces blood pressure by combating the volume and vasoconstrictive components of moderate hypertension.

## Antihypertensive effectiveness

To maximize therapeutic effects and minimize side effects Regroton provides 50 mg. of long-acting chlorthalidone plus the clinically recommended 0.25 mg. dose of reserpine.<sup>1,2</sup>

## One-tablet-a-day convenience

When titration establishes the desirability, Regroton offers your patient a simple once-a-day regimen for increased compliance and greater economy.

# Regroton<sup>®</sup>

Each tablet provides chlorthalidone USP 50 mg., reserpine USP 0.25 mg.

## matches medication to mechanism

References: 1. Freis, E.D. The treatment of mild hypertension, Med. Times 103:63, 1975. 2. Kaplan, N.M.: When hypertension is mild or moderate. Drug Ther. 5:43, June 1975.

ic, especially with brisk diuresis, when severe  
sis is present, or during concomitant use of cor-  
teroids or ACTH. Interference with adequate  
electrolyte intake will also contribute to hypokale-  
mic digitalis therapy may exaggerate metabolic  
effects of hypokalemia especially with reference to  
cardiac activity. Any chloride deficit is generally  
and usually does not require specific treatment  
but under extraordinary circumstances (as in  
disease or renal disease). Dilutional hypona-  
tremia may occur in edematous patients in hot  
weather. Hyperuricemia may occur or gout be pre-  
cipitated in certain patients. Insulin requirements in  
diabetic patients may be increased, decreased, or  
unchanged and latent diabetes mellitus may  
become manifest. Chlorthalidone and related drugs  
decrease arterial responsiveness to norepi-  
nephrine. Chlorthalidone and related drugs may  
decrease serum PBI levels without signs of thyroid  
dysfunction. Use Regroton cautiously in patients

with ulcerative colitis or gallstones (biliary colic may  
be precipitated). Bronchial asthma may occur in sus-  
ceptible patients. **Adverse Reactions:** The drug is  
generally well tolerated. The most frequent adverse  
reactions are anorexia, nausea, vomiting, gastric irri-  
tation, diarrhea, constipation, headache, dizziness,  
weakness, muscle cramps, nasal congestion, drow-  
ziness and mental depression. Other potential side  
effects include skin rash, urticaria, ecchymosis;  
hyperglycemia and glycosuria (diabetics should be  
checked regularly), hyperuricemia and acute gout,  
and impotence. With chlorthalidone: restlessness,  
transient myopia; dysuria, orthostatic hypotension  
(may be potentiated by alcohol, barbiturates or nar-  
cotics), rare idiosyncratic reactions such as aplastic  
anemia, leukopenia, thrombocytopenia, agranulocy-  
tosis, purpura, necrotizing angitis and Lyell's syn-  
drome (toxic epidermal necrolysis); pancreatitis  
when epigastric pain or unexplained G.I. symptoms  
develop after prolonged administration; other reac-

tions reported with this class of compounds include  
jaundice, xanthopsia, paresthesia, and photosensi-  
tization. With reserpine: angina pectoris, brad-  
ycardia, ectopic cardiac rhythms (especially with  
digitalis); blurred vision, conjunctival injection, uvei-  
tis, optic atrophy, glaucoma, deafness, increased  
gastric secretions, dull sensorium, paradoxical anxi-  
ety, nightmares, reversible paralysis agitans syn-  
drome, dyspnea, weight gain, dryness of mouth,  
increased susceptibility to colds, decreased libido,  
skin flushing and pruritus. **Dosage:** Should be deter-  
mined by individual titration. (See box warning.) Dos-  
age for most patients is one tablet once a day.  
**How Supplied:** Pink, round, single-scored tablets in  
bottles of 100 and 1000.

**USV  
LABORATORIES**

USV Laboratories Inc.  
Manati, P.R. 00701

# Famous Fighters



**JOHN L. SULLIVAN**  
Bare-knuckles heavyweight champion  
1882-1892

## NEOSPORIN® Ointment (polymyxin B-bacitracin-neomycin) is a famous fighter, too.

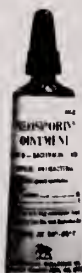
Provides overlapping, broad-spectrum antibacterial action to help combat infection caused by common susceptible pathogens (including staph and strep).

Each gram contains Aerosporin® brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base), special white petrolatum qs in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

**INDICATIONS:** Therapeutically (as an adjunct to systemic therapy when indicated) for topical infections, primary or secondary, due to susceptible organisms, as in: • infected burns, skin grafts, surgical incisions, otitis externa • primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia) • secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis) • traumatic lesions, inflamed or suppurating as a result of bacterial infection.

Prophylactically, the ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing. **CONTRAINDICATIONS:** Not for use in the eyes or external ear canal if the eardrum is perforated. This product is contraindicated in those individuals who have shown hypersensitivity to any of the components.

**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to



neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended. **PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs. **ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



Your wife had twins...



LISTA DE ANUNCIANTES

- |                          |                 |
|--------------------------|-----------------|
| 1. BELTONE ELECTRONICS   | HEARING AIDS    |
| 2. BURROUGHS WELLCOME    | NEOSPORIN OINT. |
| 3. CIBA PHARM.           | VIOFORM - HC    |
| 4. PENNWALT              | ZARAXOLYN       |
| 5. ROCHE LAB.            | LIBRIUM, VALIUM |
| 6. W. H. RORER           | CAMALOX         |
| 7. SMITH, KLINE & FRENCH | DYAZIDE         |
| 8. UPJOHN                | TPLINASE        |
| 9. U. S. V.              | REGROTON        |

# BOLETIN ASOCIACION MEDICA DE PUERTO RICO



THE FRANCIS A. COUNTRYWAY  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET  
BOSTON, MASS. 02115

**VOL. 69**

**Marzo 1977**

**No.3**



# A character all its own.



Valium (diazepam) is a benzodiazepine with a character all its own.

Pharmacologically, it has been described as more potent mg-per-mg than other available anxiolytic benzodiazepines. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> (diazepam)<sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

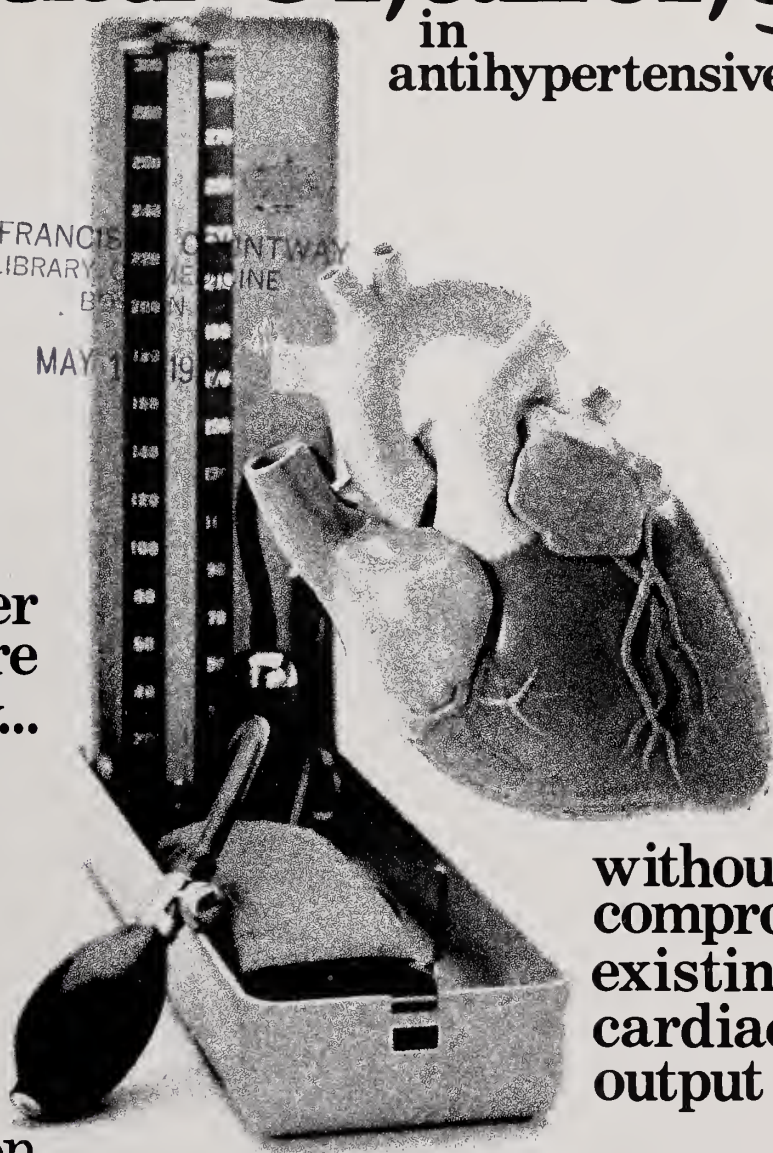


# A Dual Challenge

in  
antihypertensive therapy

THE FRANCIS & TAYLOR  
LIBRARY  
MAY 19 1974

to lower  
blood pressure  
effectively...



without  
compromising  
existing  
cardiac  
output

in hypertension

TABLETS: 250 mg, 500 mg, and 125 mg

## ALDOMET<sup>®</sup> (METHYLDOPA | MSD)

helps lower blood pressure effectively...  
usually with no direct effect on  
cardiac function—cardiac output  
is usually maintained

ALDOMET is contraindicated in active hepatic disease, hypersensitivity to the drug, and if previous methyldopa therapy has been associated with liver disorders. It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

or a brief summary of prescribing information, please see following page.

in hypertension

# ALDOMET<sup>®</sup>

(METHYLDOPA|MSD)

helps lower  
blood pressure  
effectively...  
usually with no  
direct effect on  
cardiac function—  
cardiac output is  
usually maintained



**Contraindications:** Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity.

**Warnings:** It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

**Use in Pregnancy:** Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

**Precautions:** Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

**Adverse Reactions:** *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

*Cardiovascular:* Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

*Gastrointestinal:* Nausea, vomiting, distention, constipation, flatulence, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

*Hepatic:* Abnormal liver function tests, jaundice, liver disorders.

*Hematologic:* Positive Coombs test, hemolytic anemia. Leukopenia, granulocytopenia, thrombocytopenia.

*Allergic:* Drug-related fever, myocarditis.

*Other:* Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

**Note:** Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

**How Supplied:** Tablets, containing 125 mg methyldopa each, in bottles of 100; Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486 J6AM07 (707)

**MSD** MERCK SHARP & DOHME



100 mg

250 mg

500 mg



# **Tolinase<sup>®</sup>**

**tolazamide, Upjohn**

Please contact your Upjohn representative for additional product information.

**Upjohn**

J-5695-6

© 1977 THE UPJOHN COMPANY



Organo Oficial

Fundado en 1903

Volumen 69

Marzo 1977

Número 3

## JUNTA EDITORA

José L. Cangiano, Presidente; Herman J. Flax; Norman I. Maldonado; F. Hernández Morales; Francisco Olazábal, Jr.; Nathan Rifkinson; Enrique O. Velez García; Antonio J. Grillo; Mario R. García Palmieri; Rafael Villavicencio Jiménez; E. A. Santiago Delpín; Ramón H. Bermúdez; Manuel Martínez Maldonado; José Juan Corcino; Jesús M. Vázquez; Oswaldo Ramírez Muxó.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

### Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

### Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

### Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

## CONTENIDO

Heroin Overdose on the Rise Again? (Toxicology of Morphine) .....	77
<i>Sidney Kaye, PhD and Alma Tudó de Lewis, MSc.</i>	
Management of Long Segment Esophageal Atresia .....	83
<i>Pedro J. Rosselló, MD</i>	
Diarreas Infecciosas Agudas - Diagnóstico y Tratamiento .....	87
<i>Carlos H. Ramírez Ronda, MD, FACP, Carlos León-Valiente, MD y Ramón H. Bermúdez, MD</i>	
Rehabilitación — Filosofía, Alcance y Campo de Acción .....	96
<i>Herman J. Flax, MD, FACP</i>	
Noticias .....	100

PORTADA: Caleta San Juan (Puerta de San Juan)

Cortesía: Dr. Rafael E. Ramírez

# HEROIN OVERDOSE ON THE RISE AGAIN? (TOXICOLOGY OF MORPHINE)

Sidney Kaye, Ph.D.

Alma Tudó de Lewis, MSc.

**M**orphine and its derivative heroin (diacetyl morphine) has been of great interest to us, especially during these last fifteen years. We have (just) lived through a serious epidemic of deaths due to overdose (1964-1971), which peaked in 1970 and 1971, then dipped to a low in 1973. But it now looks like this is on the rise again. See Graph I.

Opium, the dried milky juice extract from the unripe oriental poppy seed (*Papaver Somniferum*) has been in continuous use for at least several thousand years (1). Morphine the purified active ingredient of opium is still used as the standard against which newer morphine substitutes are measured. "Many of the newer agents may be considered its equal, but it is doubtful that any of them is clinically superior" (1).

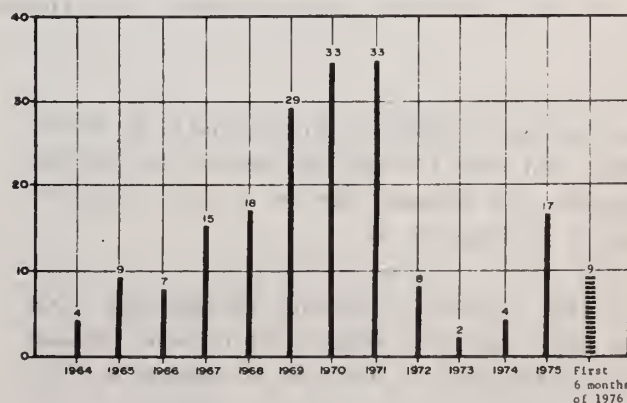
The capacity of opium to produce physical and psychological dependencies was known to the early Greeks (1). The great attraction to the use and abuse of morphine lies in its fantastic ability to tolerate pain by perhaps raising its threshold, to produce euphoria and to provide relief from misery and despair.

Opium smoking during 1750 to 1850 became very popular in the orient. In Europe during this same period "opium eaters" (drinking Laudanum) was the vogue. The unrestricted availability of opium spread to the United States where Laudanum, and Browns mixture (crude opium) sold as a "cure for all". The situation became so bad that a diacetyl derivative of morphine was synthesized supposedly as a safer and more acceptable substitute. This substitute was called "Heroin", which turned out to be about 5 x more potent than morphine and the scene was now

ripe for the enactment of the Harrison Act of 1914, which for the first time restricted and regulated the production, distribution and use of all morphine-like products in the United States.

The morphine (heroin) problem during the early half of the twentieth century then became somewhat stabilized and was mostly confined to the very poor and the very (idle) rich — up until 1960 when a "youth social revolution" took place among the middle classes. One of its manifestations was heroin abuse. Now most of us who heretofore were not involved and were indifferent, quickly become involved and very much concerned. The infamous (1960-1970) abuse of heroin became epidemic and resulted in very many deaths due to overdose. In New York City it was reported to be the No. 1 cause of death due to poisoning (2, 3).

Although Puerto Rico had a slight delay in onset,



From the School of Medicine, Institute of Legal Medicine, University of Puerto Rico.

In partial fulfillment of the requirements for the MSc. in Toxicology; the Department of Pharmacology and Toxicology, and the Institute of Legal Medicine, University of Puerto Rico.

Graph I

TABLE I  
APPROXIMATE COMPARISON

	Meperidine	Morphine	Methadone
Synonyms	Demerol; Pethidine; isonipercaine	-----	Adanon; Amidone; Dolaphine
Source	synthetic	natural	synthetic
Pupils	normal or dilated	pin-point	pin-point (moderate)
Euphoria	moderate	marked	rare (oral)
Dose (Therap.)	50-100 mg	5 - 15 mg	5 - 10 mg
Route	oral; IM	all routes	oral
MLD * (non tolerant)	1 gm	200 mg	75 mg
MLD (Tolerant)	4 gm	2 gm	500 mg
Antagonist	Naloxone or Nalorphine	Naloxone or Nalorphine	Naloxone or Nalorphine
Duration of action to prevent withdrawal Sx	5 hours	5 hours	24 hours
Dependency liability	moderate	marked	moderate
Tolerance **	moderate	marked	moderate

\* MLD: minimum lethal dose

\*\* Tolerance is lost after a period of abstinence. This is a frequent cause of death due to "accidental" overdose.

we did however follow the general trend of the United States and after a couple of years, we too felt the tragedy of it becoming our No. 1 cause of death \* due to poisoning (4, 5).

Graph 1 shows an alarming increase from 1964 to 1970 (and 1971) when it hit its peak; followed by a sudden drop in death due to overdose in 1972,

with a low in 1973 \*. The 1974 small upturn apparently was significant when followed with 17 reported overdose deaths during 1975. This is terrifying! Is the "horrible" epidemic on its way back?

Since the problems of morphine and its synthetic derivatives appear to be still with us; and since the (acute) diagnosis and withdrawal symptoms are not

\* Parathion was our No. 1 cause of death for many years; in 1971 parathion and morphine were tied for first place; in 1972 alcohol took first place (4, 5).

\* Note: Turkey stopped cultivating poppies in 1972 and restarted again in 1974. These figures represent only those cases that were sent to the Institute of Legal Medicine for study.



TABLE II  
APPROXIMATE COMPARISON OF VARIOUS DRUGS OF ABUSE

	Therapeutic dose	MLD	Tolerance	Withdrawal symptoms
Organic solvents	varies	varies	none	none
Amphetamine	5-10 mg	200 mg	2,000 mg	mild
Cocaine	none	500 mg	2,000 mg	none
Marihuana	none	high	none (reverse) (tolerance)	none
LSD	none	0.5 mg	100 → 2000 ug	none
Morphine	15 mg	200 mg	2000 mg	++++
Barbiturates	100 mg *	1-6 gm	500 mg	++++
Minor tranquilizers	varies	varies	none	+++
Major tranquilizers	varies	varies	none	none
Alcohol (ethyl) (whiskey)	30 ml	800 ml	moderate	+++++

\* Tolerance for barbiturates increases approximately 5 fold but the Minimum Lethal Dose (MLD) does not apparently increase.

always clear and simple; the following brief resume on the Toxicology of Morphine (heroin) is offered as a refresher.

### Morphine $C_{17}H_{19}NO_3$

**Homologues:** Dried resinous fluid (opium) of the unripe poppy seed may contain approximately 10 percent morphine and 0.5 percent codeine. Laudanum and Brown's mixture are elixers of crude opium. Heroin (diacetylmorphine); Dilaudid (hydromorphine); Numorphan (oxymorphine); Metopan (methyl dilaudid); codeine (methyl morphine).

**Uses:** Analgesia, sedation, hypnosis, and narcosis.

**Properties:** Basic, alkaloid, white crystalline, bitter

taste, MP, 254° C. Slightly soluble in ethanol; or chloroform: isopropanol (3:1), at buffered pH 8.5 - 9.5.

**MLD:** Morphine approximately 200 mg for a 150 pound man; codeine is about one-fifth as toxic; heroin is about five times more toxic. Blood levels: Therapeutic 0.01 mg percent; lethal 0.1 mg percent (non addict).

**Remarks:** Death may occur within 2 hours; but more usually within 8 hours; occasionally is delayed 24 hours. If patient survives 48 hours, prognosis is good.

**Symptoms (acute):** Pinpoint pupils, powerful CNS depressant, decreased mental concentration, euphoria, elevated pain threshold, stimulation of imagination and freedom from anxiety; sweating, loss of senses to time and space, no hunger sensation, nausea and vomiting, constipation, itching of skin, dry mouth,

slow shallow respiration, cyanosis, pulmonary edema, cardiovascular depression, shock, marked respiratory depression (Cheyne-Stokes), until anoxia occurs, face markedly congested and cyanotic, deep coma, areflexia, respiratory failure, death. Pupils may dilate as death approaches.

*Withdrawal (abstinence syndrome) (chronic) (6):* May start to appear about 4 to 8 hours after the last dose, reaching peak intensity between 36-72 hours. Lacrimation, rhinorrhea, yawning and sweating appear early followed by a restless sleep. At about 20 hours, gooseflesh \*, dilated pupils, agitation, and tremors may appear. The peak of distress during the second and third day may include insomnia, chills, weakness, intestinal cramps, nausea, vomiting, diarrhea, violent yawning, muscular aches in legs, severe low back pain, elevated blood pressure and pulse rate, sweating, dehydration which may become severe and serious producing cardiovascular irregularities. This withdrawal episode may last up to 10 days; but at any time during this period if an opiate (or related drug) is given, the symptoms disappear dramatically.

*Dependency, tolerance and compulsion (6, 7):* This is a true physiologic dependency and although withdrawal symptoms are quite severe, death is a rare consequence.

*Tolerance* is rapidly acquired, where now it requires many times the original dose to satisfy or to hold off withdrawal symptoms. This tolerance is lost following abstinence for several weeks.

*Compulsion* is powerful to seek satisfaction and/or to abort the impending withdrawal symptoms. The degree of compulsion (and compliance) varies very widely. Much depends upon the socio-economic, psychological and mental make-up of each individual (8).

### Determinations (17)

#### Comments:

---

\* "Goose pimples" - skin like a plucked turkey ("cold turkey").

- (1). Heroin (di acetyl morphine) is metabolized in man almost completely to morphine.
- (2). Codeine (methyl morphine) is metabolized only partly to morphine.
- (3). The morphine metabolite then conjugates (90 percent) almost entirely to its glucuronide.
- (4). Acid hydrolysis may increase the chances of detecting trace amounts many hours after exposure.
- (5). Specimens of choice are urine and bile. Bile contains much more morphine per unit volume but is very troublesome to extract.
- (6). Chloroform: isopropanol (3:1) is the solvent of choice.
- (7). Separation by adsorption is not as effective as direct solvent extraction, but adsorption however, lends itself to multiple sample analysis.
- (8). Separation techniques in order of effectiveness:
  - (a). Solvent: Chloroform: isopropanol (3:1) (best).
  - (b). Amberlite XAD extraction cartridge (Brinkmann).
  - (c). Norit charcoal.
  - (d). Reeves cation paper extraction: Reeve angel grade SA-2 ion exchange resin loaded paper cut in 6 x 6 cm square (least).
- (9). The mere finding of morphine in urine or bile if not supported by a good history and supporting pathology, is not sufficient proof of death due to overdose. An addict with high tolerance can have quite high urinary morphine levels and yet not be "over dosed".
- (10). On the other hand, negative findings do not always rule out death due to overdose because some non addicts are very sensitive to small amounts; and also metabolism during a long survival period, or a rapid death following injection may not always permit easy detection.
- (11). Detection and determination may be made by:
  - (a). Thin Layer Chromatography (TLC).
  - (b). Immunoassay
    1. Enzyme Mediated Immunoassay Technique (EMIT).
    2. Radio Immunoassay (RIA).
  - (c). Gas Chromatography (GC).

## Treatment

Immediate action is necessary to maintain all vital signs. Maintain respiration with a patent airway and artificial respiration. Clear with suction if necessary to maintain a patent airway. Maintain blood pressure, body heat, water, and electrolyte balance. Support against shock and pulmonary edema.

Naloxone is the specific antagonist of choice. Nalline or Lorfon may also be used with caution but they may produce further depression if morphine or derivatives were absent.

These antagonists are very effective. They can reverse a fall in blood pressure, and can decrease pulse rate, and cardiac arrhythmia when these are produced by morphine or derivatives. Loss of superficial and deep reflexes, corneal and gag reflexes, pupillary constriction return to normal within 5 minutes. These dramatic changes may further confirm the presence of morphine or derivative, but *do not* remove the dangers of emergency. Most often treatment must be repeatedly given (as needed). Close observation is required for 24 hours.

Since these antagonists inactivate action of morphine, they can also provoke withdrawal symptoms in those persons addicted to morphine (or its derivatives).

Symptoms and treatment for Demerol, Methadone, Heroin, Codeine, Metapon, generally are similar to Morphine.

## Summary

Death due to Morphine (heroin) overdose had been a very serious problem during 1965 to 1972. In 1971 it became the number one cause of death due to poisoning in Puerto Rico.

Suddenly in 1972 we had a steep drop in death rate which continued in 1973. However, in 1974 and 1975 death due to morphine (heroin) appeared to be on the rise again.

Will this trend upward continue?

Since the problems of morphine and its derivatives appear to be still with us, a brief resume on its homologues, minimum lethal dose, general methods and interpretation of blood and urine analysis, symptoms (acute and withdrawal), and general treatment is offered as a guide.

## Resumen

La muerte por sobredosis de morfina (heroína) fue un problema serio durante los años del 1965 al 1972. Para el año 1971 fue la primera causa de muerte en Puerto Rico por envenenamiento.

Súbitamente en el 1972 hubo una baja en las muertes, la cual continuó hasta el 1973. Sin embargo en los años 1974 y 1975, la muerte debido a morfina (heroína) vuelven a aumentar otra vez.

¿Continuarán subiendo los casos?

Debido a que los problemas con morfina (heroína) y sus derivados siguen; un resumen breve de sus homólogos, dosis mínima letal, síntomas (agudos y dejamiento), método general e interpretación de esos resultados, y tratamiento general se señalan como guía.

Información detallada y métodos analíticos están disponibles al solicitar un re-impreso.

## References

1. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics, the MacMillan Co., New York, 3rd. Ed., 1965.
2. Helpern, Milton: Fatalities from narcotic addiction in New York City, Hum. Path., 3: 13, 1972.
3. Baden, Michael, Deputy Chief Medical Examiner of New York City: Personal communications.
4. Kaye, Sidney: Patterns of poisoning in Puerto Rico. Bol. Asoc. Med. de P. R., 62: 18, 1970.
5. Kaye, Sidney: Changing patterns of poisoning in Puerto Rico. Bol. Asoc. Med. de P. R., 66: 64, 1974.
6. Goth, A.: Medical Pharmacology, C. V. Mosby Co., St. Louis, 6th. Ed., 1972.
7. Cutting, W.: Handbook of Pharmacology, Meredith Publ. Co., New York, 4th. Ed., 1969.
8. Wald, P. M., & Hutt, P. B., Co-Chairman: Dealing with drug abuse, A report to the Ford Foundation, Praeger Publ., New York, 1973.
9. Dreisbach, Robert H.: Handbook of poisoning and treatment, Lange Medical Publ., Los Altos, Cal., 7th. Ed., 1972.
10. Meyers, F. H., Jawetz, E., Goldfien, A.: Review of Medical Pharmacology, Lange Med. Publ., Los Altos, Cal., 4th. Ed., 1974.
11. Kaye, Sidney: Emergency Toxicology. C. C. Thomas. Springfield, Ill., 3rd. Ed., 1973. 2nd. Printing.
12. Kupferberg, H. J., Burkhalter, A., Way, E. L., Journ. Pharm. Exp. Ther., 145: 247, 1964.
13. (a). Davidow, B., Petri, Quame, Tech. Bull. Reg. Technol., 38: 298, 1968.  
(b). Davidow, B., Petri, Quame, Searle, Fastlich, Savitzky, Am. J. Clin. Path., 46: 58, 1966.



14. Mule, S. J., *Anal. Chem.*, 36: 1907, 1964.
15. Steel, J., *Journ. Chrom.*, 19: 300, 1965.
16. Curry, A.: *Poison Detection*, C. C. Thomas, Springfield, Ill., 2nd. Ed., 1969.
17. Tulo de Lewis, A.: Thesis (M.Sc.), Med. Sci. Campus, Univ. of P. R., 1972.
18. Lorenzo, B.: *Methodology for analytical toxicology*, Sunshine, II, Ed. (Immunoassay of Drugs), CRC Press, Cleveland, Ohio, 1975.
19. Mule, S., Sunshine, I., Braude, M., Willette, R., Eds.: *Immunoassay of Drugs*, CRC Press, Cleveland, Ohio, 1974.
20. Clarke, E. G. C.: *Isolation and identification of drugs*. Pharmaceutical Press, London, 1969.

# MANAGEMENT OF LONG SEGMENT ESOPHAGEAL ATRESIA

Pedro J. Rosselló, MD

**E**sophageal atresia and tracheoesophageal fistula is one of the true emergencies in neonatal surgery. Several non-surgical factors are related to the chances of survival in these newborns: type of atresia, size and gestation of the baby, associated congenital anomalies (2, 3). A marked improvement in survival was recorded after the description of a primary repair for this anomaly (1). Today, primary repair in the newborn period with an end to end anastomosis remains the best approach to esophageal atresia.

Cases of long segment atresia are not amenable to this straight-forward approach, and presently remain a major surgical challenge. In these children the esophageal segments cannot be brought together without undue tension. This situation exists in a large percentage of Type A esophageal atresia, and in a smaller percentage, but significant number of the common Type C atresia.

## Methods Used in Management of Long Segment Esophageal Atresia

Placement of the stomach in the thorax with direct anastomosis has resulted in a high incidence of reflux esophagitis, aspiration, pneumonia, and failure to thrive, making this alternative a poor one. Several methods based on elongation of the esophageal pouches have been attempted. Howard and Myers first described this, using a mercury bougie (4). This was subsequently tried with success by other groups (5, 6). An interesting modification was reported by Hendren

(7, 8) using magnets and an electromagnetic field to carry out the stretching of the segments. These approaches all have major disadvantages; prolonged hospitalization required for the elongation phase (4-13 weeks), a high incidence of anastomotic leaks and strictures (6). In addition the magnetic approach requires very expensive equipment, which is not easily available to most institutions (8).

Organ replacement has been the most extensively used approach. Of these, coloesophagoplasty is the most common. Several techniques using right or left colon for the conduit, creating a preliminary cervical esophagostomy or tube pharyngostomy, utilizing an early operative approach or a delayed staged one, have been described (9, 10, 11, 12, 13). Although these usually provide a very adequate conduit in many cases, significant problems persist: recurrent aspiration, anastomotic strictures which are particularly difficult to dilate; peptic ulceration at the cologastrostomy site; redundancy, dilatation, and stasis of the interposed colon, many times leading to growth failure and malnutrition. The jejunum has been utilized less frequently as a prosthesis because problems with blood supply limit the mobilization of this tube. Gastric tube esophagoplasty has been advocated (14-16). This has the advantage of better emptying, less peptic esophagitis, and easier dilatation of strictures. All these organ esophagoplastics require staging and therefore prolong hospitalization, increase the number of operative procedures, and require extended esophageal drainage and gastrostomy feedings.

Other ingenious methods have been devised to deal with a long esophageal gap, using a suture fistula (17, 18) or intraluminal clamps (17, 19) to join the widely separated ends. These carry a significant risk of mediastinitis and sepsis, and commits the child to a prolonged course of postoperative dilatations for the invariable strictures that form.

Because of the problems encountered with all these techniques, experimental studies on the use of esophageal myotomy have been carried out. A preliminary

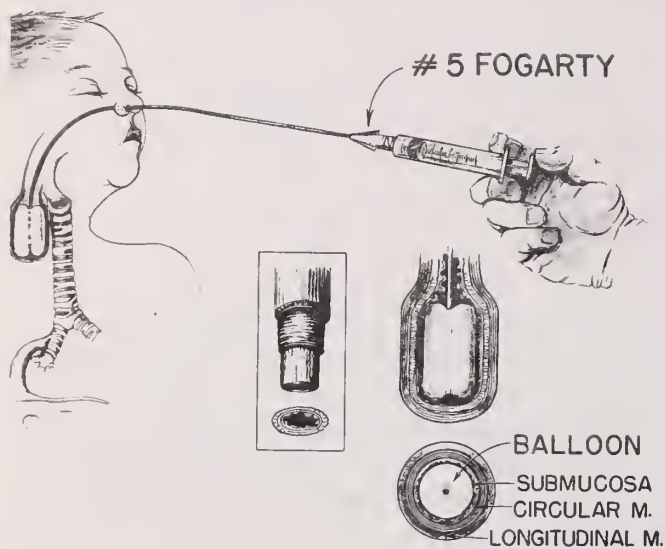


Figure 1: A no. 5 Fogarty catheter is introduced transnasally into the upper esophageal pouch. By inflating the balloon a smooth surface is provided to cut the longitudinal and circular muscle layers without damaging the underlying submucosa.

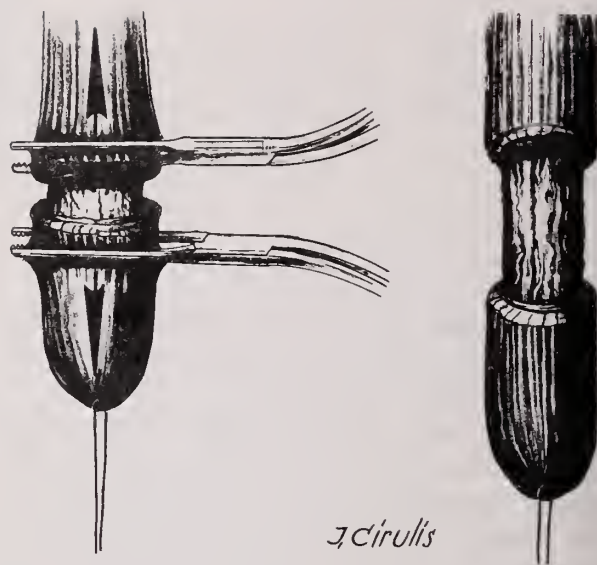


Figure 3: Once the myotomy is completed, non crushing vascular clamps are applied above and below the myotomy and gentle stretching is carried out. Note that the main blood supply is left intact in the submucosal layer.

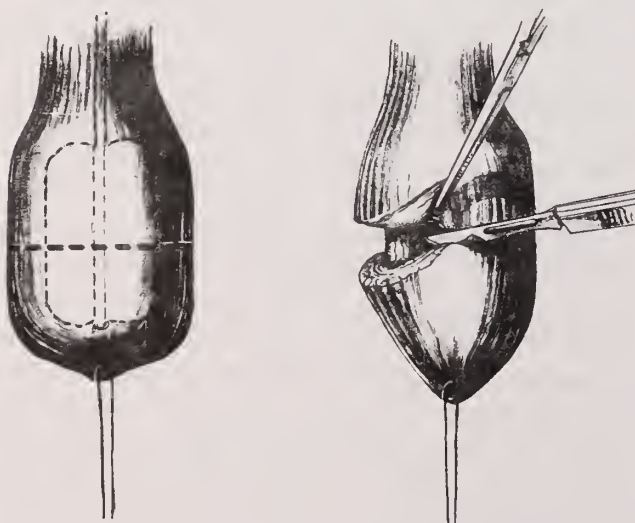


Figure 2: A circular transverse incision in the muscular layers is carried out 2 cm. from the bottom of the pouch.

series of experiments defined the important factors in reconstruction of the esophagus (20-25). Everting anastomoses were shown to result in stricture (21). The significance of differences in suture placement though the various layers of the esophageal wall was noted to be minimal (22). The most important factor in stricture formation is the magnitude of mucosal defects (23, 24, 25). Muscular interruptions, on the

other hand, cause negligible fibrosis and do not result in either organic or functional obstructions (25). Based on these findings, experiments to reduce the tension of esophageal anastomosis were conducted in piglets (26, 27). It was shown that a 60-70 percent decrease in approximating force could be obtained by performing a circular myotomy of the esophagus (26). The muscle distal to the myotomy is preserved without changes since the main blood supply runs in the submucosal layer. In the normal esophagus there is no interruption of the peristaltic wave beyond the myotomy (26). This technique was first applied to children with esophageal atresia by Livaditis in Sweden (28) and first described clinically in the U. S. by Eraklis, Rossello, and Ballantine (29). The latter group described a modification that makes the procedure technically simpler.

### Technique of Myotomy

After it is determined at operation that a primary anastomosis cannot be completed without undue tension steps are taken to perform a myotomy. (Figure 1) A no. 5 Fogarty Catheter is introduced into the upper pouch and inflated, to provide a smooth circum-





Figure 4: Barium swallow in the immediate postoperative period after circular myotomy and end to end anastomosis. Note the adequate anastomosis site, absence of leaks or stricture, and a slight bulging of the upper pouch at the myotomy site.



Figure 5: Barium swallow, three months follow-up.

ferential surface to divide the longitudinal and circular muscle fibers. With the aid of magnification glasses, the myotomy is carried out transversely approximately 2 cm. from the trough of the upper pouch (Figure II). Vascular clamps are placed to stretch the mucosa by gentle traction (Figure III). The anastomosis to the lower segment is then completed as usual.

## Discussion

Using the circular myotomy technique gaps of up to 5 cm. have been bridged (28, 29). This method has the advantages of a primary end to end repair using only esophageal tissue, and circumvents many of the disadvantages of the other methods discussed. Hospitalization time is shortened, the number and magnitude of operative procedures is reduced. It provides the child with an immediate and adequate conduit utilizing only esophageal segments. Radiologic studies show function equivalent to the standard end to end anastomosis (Figures IV, V) and there does not appear to be any increase in the occurrence of leaks or strictures in the small number of cases reported. Longterm survivors of repaired esophageal atresia have shown a constant and persistent motility abnormality of the esophagus (30). This is congenital in origin, the dysfunction preceding any surgical intervention. Whether the addition of an upper pouch myotomy will result in greater dysmotility is not presently known. However in studies with the normal esophagus a myotomy does not alter the function significantly (26). In both of the reported clinical series the immediate postoperative function is similar to that of standard primary anastomosis.

In summary, circular esophagomyotomy is a technically feasible and widely applicable method to deal with the difficult problem of long segment esophageal atresia. It offers many advantages over other approaches. Initial results are comparable to those of standard primary anastomosis. It is a technique that should be an integral part of the armamentarium of the surgeon dealing with congenital anomalies of the newborn.

## Summary

The surgical management of long segment esophageal atresia is discussed. Several approaches to this pro-

blem are reviewed. A new technique utilizing a circular esophagomyotomy is presented.

## References

1. Haight, C., Towsley, H. A.: Congenital Atresia of the Esophagus with tracheoesophageal atresia. *Surg. Gyn. & Obst.* 76: 672, 1943.
2. Holder, T. M., Cloris, D. I., Lewis, J. E., Pilling, G. P.: Esophageal atresia and tracheoesophageal fistula. *Pediatrics* 34, 542, 1964.
3. Hays, D. M., Woolley, M. M., Snyder, W. H.: Esophageal Atresia and tracheoesophageal fistula: Management of uncommon types. *J. Pediat. Surg.* 1, 240, 1966.
4. Howard, R., Myers, N. A.: Esophageal atresia: A technique for elongating the upper pouch. *Surgery* 58: 725, 1965.
5. Johnson, P. W.: Elongation of the upper segment in esophageal atresia: Report of a Case. *Surgery* 58: 741, 1965.
6. Mahour, G. H., Woolley, M. M., Gwinn, J. L.: Elongation of the upper pouch and delayed anastomotic reconstruction in esophageal atresia. *J. Pediat. Surg.* 9, 373, 1974.
7. Hendren, W. H., Hale, J. R.: Electromagnetic bouginage to lengthen esophageal segments in congenital esophageal atresia. *N. Eng. J. Med.* 293: 428, 1975.
8. Hendren, W. H., Hale, J. R.: Esophageal atresia treated by electromagnetic bouginage and subsequent repair. *J. Pediat. Surg.* 11, 713, 1976.
9. Talbert, J. L., Haller, J. A.: Temporary tube pharyngostomy in the staged repair of congenital tracheoesophageal fistula. *Surgery* 58: 737, 1965.
10. Waterston, D. J.: Colonic replacement of the esophagus. *Surg. Clin. N. Am.* 44: 1441, 1964.
11. De Boer, A.: Retrosternal colonic substitute in children. *Surg. Clin. N. Am.* 44: 1449, 1964.
12. Bently, J. F. R.: Primary Colonic substitution for atresia of the esophagus. *Surgery* 58: 731, 1965.
13. White, J. J.: Early short segment left colon interposition for esophageal atresia. *J. Pediat. Surg.* 11, 735, 1976.
14. Heimleisch, H. J.: The use of a gastric tube to replace or bypass the esophagus. *Surgery* 37: 549, 1965.
15. Burrington, J. D., Stephens, C. A.: Esophageal replacement with a gastric tube in infants and children. *J. Pediat. Surg.* 3: 246, 1968.
16. Cohen, D. H., Middleton, A. W., Fletcher, J.: Gastric tube esophagoplasty. *J. Pediat. Surg.* 9: 451, 1974.
17. Rehbein, F., Schweider, N.: Reconstruction of the esophagus without colon transplantation in cases of atresia. *J. Pediat. Surg.* 6: 746, 1971.
18. Shafer, A. D., David, T. E.: Suture fistula as a means of connecting upper and lower segments in esophageal atresia. *J. Pediat. Surg.* 9: 669, 1974.
19. Okmian, L., Livaditis, A., Bjorck, G., Ivenmark, B.: Esophageal Clamp anastomosis. *Scand. J. Thor. Cardiovasc. Surg.* 3: 151, 1969.
20. Livaditis, A., Ivenmark, B.: Esophageal anastomosis in piglets. *Scand. J. Thor. Cardiovasc. Surg.* 3, 174, 1969.
21. Kornfalt, S. A., Okmian, L., Jonsson, N.: Everted and end esophageal anastomosis in piglets. *Zeitung Kinderchir.* 12: 304, 1973.
22. Kornfalt, S. A., Okmian, L., Jonsson, N.: Esophageal anastomosis in piglets. *Zeitung Kinderchir.* 13: 306, 1973.
23. Kornfalt, S. A., Okmian, L., Jonsson, N.: Mucosal defect and esophageal stricture formation. *Zeitung Kinderchir.* 13: 392, 1973.
24. Kornfalt, S. A., Okmian, L., Jonsson, N.: Healing of circular esophageal mucosal defects. *Zeitung Kinderchir.* 13: 184, 1973.
25. Livaditis, A., Okmian, L., Bjorck, G., Ivenmark, B.: Esophageal suture anastomosis. *Scand. J. Thor. Cardiovasc. Surg.* 3: 163, 1969.
26. Livaditis, A., Radberg, L., Odensjo, G.: Esophageal end to end anastomosis: Reduction of anastomotic tension by circular myotomy. *Scand. J. Thor. Cardiovasc. Surg.* 6: 206, 1972.
27. Kornfalt, S. A., Okmian, L., Jonsson, N.: Healing of esophageal anastomosis after release of tension by myotomy. *Zeitung Kinderchir.* 12: 444, 1973.
28. Livaditis, A.: Esophageal atresia: A method of overbridging large segmental gaps. *Zeitung Kinderchir.* 13: 298, 1973.
29. Eraklis, A. J., Rossello, P. J., Ballantine, T. V. N.: Circular esophagomyotomy of upper pouch in primary repair of long segment esophageal atresia. *J. Pediat. Surg.* 11: 709, 1976.
30. Laks, H., Wilkinson, R. H., Schuster, S. R.: Longterm results following correction of esophageal atresia with tracheoesophageal atresia. *J. Pediat. Surg.* 7: 591, 1972.

# DIARREAS INFECCIOSAS AGUDAS

## DIAGNOSTICO Y TRATAMIENTO

Carlos H. Ramírez Ronda, MD, FACP

Carlos León-Valiente, MD

Ramón H. Bermúdez, MD

La diarrea es uno de los problemas más comunes que nos encontramos en la práctica de la medicina tanto por el médico de familia, el pediatra, como el internista. Es una causa significativa de morbilidad en Puerto Rico y Estados Unidos y de mortalidad en los países menos desarrollados del mundo. Para simplificar y delucidar el problema de la diarrea infecciosa trataremos primero de explicar los mecanismos patofisiológicos de las diarreas y subsiguiente a esto presentar aquellos puntos y detalles en el historial, examen físico y pruebas sencillas de laboratorio que ayuden al médico a hacer una evaluación clínica del paciente y llegar a un diagnóstico etiológico más fácilmente.

En términos generales, las diarreas pueden ser causadas por dos mecanismos principales: 1) las que son mediadas por toxinas y: 2) las que son causadas por invasión de la mucosa gastrointestinal.

### Mecanismos de la Diarrea

#### *Enterotoxigenicidad:*

*Vibrio cholerae* y *Escherichia coli* enterotoxigénicos son ejemplos primarios de bacterias que cuando tienen en sus células un plásmido (partícula de material genético infectando la célula bacteriana) son capaces de secretar proteínas extracelulares o toxinas que tienen efectos dramáticos en el transporte de líquidos y elec-

trolitos en el intestino delgado. Este efecto lo hacen sin causar ningún cambio anatómico en la superficie de la mucosa. Estas enterotoxinas causan una disminución de la absorción de sodio y un aumento en la excreción de cloruro, bicarbonato y agua en volúmenes que sobrepasan la capacidad absorptiva del colon. Mientras las exotoxinas de cólera y la enterotoxina de *Escherichia coli* producen su efecto aumentando las concentraciones intracelulares de AMP cíclico, el mecanismo de acción de otras enterotoxinas bacterianas tales como las de *Clostridium perfringens*, *Vibrio parahaemolyticus*, *Staphylococcus aureus*, *Salmonella* y *Shigella dysenteriae*, Tipo I, permanece desconocido. Trabajos recientes han implicado el sistema de prostaglandinas en estos mecanismos (1).

Las pruebas de laboratorio para la determinación de producción de enterotoxina son difíciles y muchas veces contradictorias. Cuando una muestra se prueba por diferentes sistemas tales como el ileo del conejo, el ratón recién nacido o en el cultivo de tejido de las células adrenales los resultados pueden ser variados. La interpretación se hace más difícil ya que la habilidad para colonizar el intestino delgado es independiente de la producción de la enterotoxina y los serotipos clásicos (enteropatógenicos) de *Escherichia coli* pueden perder la habilidad para producir enterotoxina y convertirse, por lo tanto, en no enterotoxigénicos, mientras que otros tipos, los cuales no causaban diarrea anteriormente, pueden adquirir esta capacidad (2). Por lo tanto, un reporte de laboratorio en donde se recupere uno de los serotipos clásicos (enteropatógenicos de *Escherichia coli*) no significa necesariamente que este sea el agente causante.

Clínicamente, los pacientes con diarreas mediadas por enterotoxinas tienen un comienzo súbito de náusea, vómitos, retortijones y excremento líquido. El desbalance de líquidos y electrolitos puede ser grande y resultar en "shock" hipovolémico. Ya que la superficie de la mucosa no ha sido dañada, no se encuentra en la excreta, sangre, moco o leucocitos.

---

De la Sección de Enfermedades Infecciosas, Departamentos de Investigación y de Medicina - Hospital de Veteranos y Escuela de Medicina, Universidad de Puerto Rico, San Juan, Puerto Rico.

Copias de este artículo se pueden adquirir escribiendo a: Dr. Carlos H. Ramírez Ronda, Sección de Enfermedades Infecciosas, Hospital de Veteranos, GPO Box 4867, San Juan, Puerto Rico 00936.



### Enteroinvasión:

Organismos tales como *Shigella*, *Entamoeba histolytica* y *Yersinia enterocolitica* son agentes que se asocian al síndrome de disentería (toxemia sistémica, tenesmus y excreta en volúmenes pequeños que contiene sangre, moco y leucocitos) y este es causado por el mecanismo de invasión y disrupción de la mucosa colónica. Este mismo fenómeno se ha demostrado recientemente con ciertas cepas de *Escherichia coli* que previamente se consideraban no patogénicas (3, 4).

### Otros Mecanismos:

La presencia de parásitos tales como *Giardia lamblia* en el intestino delgado llega a causar malabsorción por mecanismos desconocidos. Se ha sugerido que un número grande de estos organismos pueden presentar una barrera física a la absorción de nutrientes y favorecer su eliminación.

Otro mecanismo que se ha descrito es el sobrecrecimiento en el intestino delgado proximal de flora anaeróbica, la cual normalmente está restringida al íleo distal; este sobrecrecimiento anaeróbico resulta en una sobreproducción de sales biliares deconjugadas, resultando en un cuadro de diarrea. Cuando el sobrecrecimiento es de organismos aeróbicos tales como los coliformes, el cuadro se ha asociado con una deficiencia secundaria de disacaridasas resultando en la diarrea osmótica, especialmente cuando el paciente ingiere comida que contenga lactosa.

Un número grande de agentes virales como los adenovirus, echovirus, coxsackie virus y reovirus han sido implicados como causa de diarrea aguda. Aunque el mecanismo es incierto se ha postulado que la infección viral inicial induce una motilidad desordenada del intestino delgado y un subsiguiente sobrecrecimiento de la flora normal resultando en el cuadro descrito anteriormente. Aunque la etiología viral ha sido frecuentemente envuelta para explicar los episodios de diarreas no bacterianas, en solo un pequeño número de casos se documenta un agente viral como etiología, usando cultivos en tejidos. Usando la técnica de microscopía electrónica de la excreta se han descubierto agentes virales que no se propagan en métodos de cultivo de tejido más pueden ser responsables de cerca del 70 por ciento de los casos de gastroenteritis aguda, no bacteriana (5). Estos agentes tienen varios nombres tales como: reovirus, orbi-

virus, duovirus y rotavirus. Estos agentes virales están distribuidos a través de todo el mundo y afectan principalmente infantes entre las edades de seis meses a 4 años. Este agente o agentes son responsables por lo que conocemos como la enfermedad de vómito del invierno en la infancia. El agente "Norwalk" y virus relacionados aparentemente son menos comunes y están asociados con brotes aislados afectando adultos y niños. El cuadro clínico incluye vómitos, pero la intensidad de fiebre y diarrea es muy variable.

Algunos pacientes con diarrea debido a estos nuevos agentes se han estudiado por biopsia intestinal. La patología es limitada al intestino delgado. Se ven cambios inflamatorios leves de la pared intestinal, vascularización de las células epiteliales y deficiencias de disacaridasas. El cuadro clínico se parece al descrito anteriormente en la diarrea bacteriana la cual es mediada por enterotoxinas.

### Diagnóstico diferencial:

El paso inicial en el diagnóstico del paciente que se presenta con diarrea, es el excluir aquellas causas de diarrea no infecciosa (Véase Tabla I). Esta diferenciación se logra basándose en el historial, examen físico y las pruebas de laboratorio apropiadas. Cuando el paciente es un infante, el médico debe estar consciente que infecciones tales como otitis media y pulmonía pueden ser acompañadas por los síntomas de excreta blanda. El segundo paso es decidir si los síntomas indican enfermedad del intestino delgado o enfermedad del intestino grueso.

La enfermedad más fácil de reconocer clínicamente es shigelosis, pero para complicar la vida un poco, shigelosis tiene dos síndromes clínicos distintos: diarrea y disentería. En la forma disentérica clásica, el paciente tiene volúmenes pequeños de excreta consistiendo de moco, con o sin sangre. Hay una febrícula baja y la víctima sufre de retortijones abdominales y tenesmo. Una muestra de excreta teñida con azul de metileno revela una cantidad grande de leucocitos. Los síntomas se empeoran en un período de 2 a 3 días y persisten sin mejoría por un período adicional, y de 7 a 10 días o más, si no se da terapia antimicrobiana específica. La forma diarreica tiene un comienzo más dramático y abrupto caracterizado por fiebre alta y postración. Los niños tienen la tendencia a tener convulsiones. La excreta es profusa en volumen y de carácter aguado. Puede contener hilachas de moco, pero si se examina bajo el microscopio se ven muy pocos polimorfo-

TABLA I  
CAUSAS MAS FRECUENTES NO INFECCIOSAS DE DIARREA

- 
- |      |  |
|------|--|
| A.   | Malabsorción   |
|      | 1. Fibrosis quística   |
|      | 2. Insuficiencia pancreática   |
|      | 3. Enfermedad Celiaca  |
|      | 4. Síndrome del intestino corto  |
| <br> |  |
| B.   | Sobrecarga Osmótica  |
|      | 1. Deficiencias primarias o secundarias de disacaridasas                                 |
|      | 2. Síndrome de Dumping   |
| <br> |  |
| C.   | Anormalidades Anatómicas   |
|      | 1. Malrotación   |
|      | 2. Enfermedad de Hirschprung   |
|      | 3. Estenosis   |
|      | 4. Impactación fecal   |
| <br> |  |
| D.   | Endocrinopatía   |
|      | 1. Tirotoxicosis   |
|      | 2. Tumores de la cresta neural (feocromocitomas, neuroblastomas, síndrome de carcinoide) |
|      | 3. Síndrome adrenal-genital  |
|      | 4. Enfermedad de Addison   |
| <br> |  |
| E.   | Misceláneos  |
|      | 1. Deficiencias inmunológicas  |
|      | 2. Enteropatía con pérdida de proteína   |
|      | 3. Acrodermatitis enteropática   |
|      | 4. Enteritis regional  |
|      | 5. Colitis ulcerativa  |
- 

nucleares. El curso natural de esta forma de shigelosis puede tomar dos rumbos. Algunos pacientes recobran rápida y dramáticamente según comenzaron su enfermedad y en término de 24 a 72 horas están completamente bien. Otros progresan de la forma diarreica a la forma disintérica. Como se ha indicado antes, la disentería se debe a daño de la mucosa colónica, mientras que en la forma diarreica es el intestino delgado el lugar primario de patología, más el mecanismo preciso se desconoce. La lista de agentes etiológicos probables puede reducirse enfocando en ciertos detalles del historial y del examen físico y por pruebas sencillas de laboratorio según se discute subsiguientemente (Véase Tabla II).

#### Historial:

Hay que dar atención a las facetas específicas en el historial del paciente tales como: edad, exposición,

época del año, complejo de síntomas, medicaciones previas, historial de viaje, etc. Estos proveen señas que ayudan para hacer el diagnóstico. Por ejemplo, un viajero que esté regresando de la región de las Montañas Rocallosas o Leningrado en la Unión Soviética, puede tener Giardiasis, mientras que en uno que regresa de Méjico, uno debe de considerar la posibilidad de Amibiasis. Si uno conoce que hay un brote específico de un organismo en la comunidad, el diagnóstico se hace más fácil y esto se ayuda manteniéndose en contacto con las autoridades de salud pública. También el saber la edad del paciente ayuda; por ejemplo, en un niño de más de un año de edad con diarrea, usted puede eliminar la posibilidad de *Escherichia coli* enteropatógena clásica y uno que tenga más de 8 años de edad no debe tener una infección por un reovirus. La *Escherichia coli* enterotoxigénica y enteroinvasiva y los agentes "Norwalk" y sus relacionados no respetan límites de edades. Durante el verano, infecciones

TABLA II  
HALLAZGOS CLINICOS COMUNES EN DIARREAS INFECCIOSAS COMUNES

	E. coli Entero toxigénico	E. coli Enteroinvasivo	E. coli Enteropatogénico	Reovirus	Shigella Int. Del.	Shigella Int. Grueso	Salmonella
Sitio de Acción	Intestino Delgado	Intestino Grueso	Intestino Delgado	Intestino Delgado	Intestino Delgado	Intestino Grueso	Intestino Delgado y Grueso
Mecanismo de Acción	Toxina Cualquier edad	Invasión Cualquier edad	< 1 año Ninguna Otoño Gradual	< 8 años Variable Invierno Súbito Común	Toxina > 2 años 50 por ciento Variable Súbito	Invasión Cualquier edad 50 por ciento Variable Gradual	Cualquier edad Variable Variable Variable
Edad	Común	No común	No común	No común	No notable	No notable	Común
Diarrea Doméstica	Raro	Presente	Ninguna	No común	102-104 <sup>o</sup> F	100-102 <sup>o</sup> F	Variable
Epoca	Ninguno	Ninguno	Ninguno	Ninguno	Ninguno	Bronquitis	Pocos
Comienzo	Ninguna	Ninguna	Ninguna	Comunes	Comunes	Ninguna	Ninguna
Vómito	Súbito	Súbito	Normal	Normal	Débil	Débil	Normal
Fiebre 102 <sup>o</sup> F	Común	No común	Moderado	Grande	Grande	Pequeño	Moderado
Síntomas respiratorios	Grande	Pequeño	Resbalosa	Acuosa	Acuosa	Viscosa	
Convulsiones	Acuosa	Viscosa		Sin olor	Sin olor	Sin olor	
Tono esfínter anal	Ninguna	Presente	Raro	Ninguna	Ninguna	Notable	
Volumen de excreta	Ninguno	Presente	Variable	Ninguno	Notable	Notable	Moderado
Consistencia de excreta	Sin color	Verdosa	Verdosa	Sin color	Sin color	Verdosa/con sangre	Verdosa
Olor de la excreta	Ninguno	Presentes	Variable	Ninguno	Ninguno	Notables	Notables
Sangre en excreta	Ninguno			Ninguna	Ninguna	Presente	Ninguna
Moco en excreta				5-7 días	1-3 días	> 7 días	3-7 días
Color de excreta	Corta						



**TABLA III**  
**TERAPIA ANTIMICROBIANA EN LAS DIARREAS DE ORIGEN**  
**INFECCIOSO**

Presentación Clínica	Agentes Etiológicos	Terapia Antimicrobiana Específica
Síndrome del Intestino Delgado	Viruses	Ninguna
	Envenenamiento por comidas con estafilococos y clostridios	Ninguna
	V. parahaemolyticus	Ninguna
	E. coli enterotoxigénico (Turista)	Desconocida
	E. coli enteropatogénico	Neomicina o Colistin PX X 5 días
	V. cholerae	Tetraciclina
	G. lamblia	Quinacrina o Metronidazole PO X 5-10 días
	E. coli enteroinvasivo	Desconocida
	Y. enterocolítica	Ninguna
Síndrome del Intestino Grueso	Shigellosis	Droga absorbible oralmente al cual el organismo es susceptible en vitro
	Salmonellosis	Ninguna en cuadro clínico común y corriente
		Infante o huésped inmunosuprimido Ampicilina o Cloranfenicol
	S. aureus	Droga antiestafilocócica parenteral (Meticilina o Nafcilina) Vancomicina PO
	Entamoeba histolytica	Diodoquin ® o Metronidazole

gastrointestinales traen a la mente los enterovirus y envenenamiento por comidas (estafilococos, clostridios, salmonelas) usualmente ocurriendo después de tener pasadías, mientras que la enfermedad del vómito del invierno es mayormente causada por los reovirus y los agentes relacionados a "Norwalk". Cuando un paciente ha sido sometido a un procedimiento quirúrgico mayor en donde recibió antibióticos de amplio espectro, el desarrollo de diarrea apunta a enterocolitis estafilocócica pseudomembranosa.

#### Examen Físico:

El examen físico debe ser dirigido a determinar el grado de deshidratación que presenta el paciente. Evidencia de pérdida de peso, determinación de presión sanguínea, evaluación del nivel de conciencia, status de la fontanela anterior, examen de la turgencia de la piel y de los ojos, a la vez que la humedad de las membranas mucosas son los puntos mayores que deben de considerarse. Esta información, además del historial, de la cantidad de líquidos que ha ingerido previamente, frecuencia de orinar y la documentación de la cantidad de líquidos perdida, ayudan a estimar el grado de deshidratación y decidir la necesidad de hospitalización.

**TABLA IV**  
**DOSIS ANTIMICROBIANA EN INFECCIONES**  
**INTESTINALES**

Droga Antimicrobiana	Dosis Adulto	Dosis Niños	Frecuencia	Vía
Ampicilina	4 gm/día	100 mg/Kg/día	4 dosis	Oral IM, IV
Amoxicilina	1.5 gm/día	40 mg/Kg/día	3 dosis	Oral
Cefalotina	2-4 gm/día	50-100 mg/Kg/día	4 dosis	IV, IM
Cloranfenicol	2 gm/día	50-100 mg/Kg/día	4 dosis	Oral IV
Colistimetato (colistina)	No indicado	10-15 mg/Kg/día	4 dosis	Oral
Diiodohydroxiquinina	2 gm/día	40 mg/Kg/día	4 dosis	Oral
Emetina	65 mg/día	1 mg/Kg/día	1 dosis	IM
Meticilina	8-12 gm/día	200 mg/Kg/día	4 dosis	IM, IV
Metronidazole				
Giardia	750 mg/día	20 mg/Kg/día	4 dosis	Oral
E. histolytica	2.25 gm/día	40-50 mg/Kg/día	4 dosis	Oral
Vancomicina	2 gm/día	50-60 mg/Kg/día	4 dosis	Oral
Tetraciclina	2 gm/día	40 mg/Kg/día	4 dosis	Oral
Sulfametoxazol	2 gm/día	50 mg/Kg/día	4 dosis	Oral
Neómicina	No indicado	100 mg/Kg/día	4 dosis	Oral
Paromicina	1.5 gm/día	25 mg/Kg/día	3 dosis	Oral

Es muy raro que el examen físico apunte hacia un diagnóstico etiológico específico como en los casos en que aparece una erupción macopopular eritematosa asociada con enterovirus. Es importante enfatizar que en los infantes una deshidratación significativa con toxemia y acidosis puede enmascarar los signos y síntomas de condiciones asociadas. Por lo tanto, debe de hacerse una investigación en detalle para encontrar otros focos de infección tales como otitis media, pulmonía y meningitis en todos los infantes con diarrea.

#### *Pruebas de Laboratorio:*

El conteo de glóbulos blancos y su diferencial usualmente no ayudan clínicamente en el diagnóstico de la enfermedad diarreica, excepto cuando se encuen-

tra una bandemia (500 bandas/mm), lo cual es muy sugestivo de shigelosis. El conteo total de glóbulos blancos puede estar aumentado, normal o anormalmente bajo en shigelosis, pero en las tres situaciones más de la mitad de los pacientes tienen de 10 a 40 por ciento de bandas en el conteo diferencial. Esto es poco usual en otros tipos de diarrea.

El examen de la excreta fresca para consistencia, volumen, moco, sangre, color y olor puede ayudar en el diagnóstico de algunos de los agentes etiológicos. Si se sospecha enfermedad del intestino grueso, uno debe de tomar una muestra del moco de la excreta mezclada con una o dos gotas de azul de metileno y examinarla bajo el microscopio para leucocitos. Los leucocitos no se ven en excreta normal ni en la excreta diarreica cuando la enfermedad envuelve el intestino delgado, y su presencia significa inflamación del intestino grueso. Por lo tanto, sugiere *shigelosis*, *salmon-*

losis, *Escherichia coli* enteroinvasivo o *amibiasis*.

En la mayoría de los casos de diarrea aguda un cultivo de excreta no está indicado ya que el paciente usualmente recuperará en unos días con solamente cuidado mínimo. Hay un grupo de situaciones en donde el cultivo de excreta es de gran ayuda en el manejo indicado.

- 1) Pacientes hospitalizados - si el paciente está lo suficientemente enfermo para requerir hospitalización, la oportunidad de conseguir un patógeno específico es mucho más grande que en el caso común y corriente de diarrea aguda.
- 2) Cuando el paciente tiene un curso persistente o de relapso. La mayor parte de las diarreas no específicas o virales demuestran definitivamente mejoría en 3 o 5 días.
- 3) Indicaciones epidemiológicas - Si el paciente ha estado expuesto a personas y situaciones que aumentan la probabilidad de tener un patógeno reconocible.
- 4) En cualquier instancia en donde la excreta sugiera enfermedad del intestino grueso y particularmente si se encuentran leucocitos en el moco teñido con azul de metileno ya que la mayor parte de los casos de diarrea aguda con enfermedad inflamatoria del colon se deben a patógenos bacterianos.

El examen para huevos y parásitos debe de llevarse a cabo en todos los pacientes que se presentan con síntomas gastrointestinales persistentes en Puerto Rico. Ciertamente, si un paciente tiene un síndrome de disentería y no se identifica *Shigella*, uno debe de considerar *Amibiasis* aunque no es común en Puerto Rico. *Giardiasis* tiene una presentación característica y usualmente el paciente se queja de que se siente lleno, de tener una sensación no agradable en el abdomen y usualmente describirá su excreta como grasosa, resbalosa o que apesta severamente. Desafortunadamente, *Giardia lamblia* se encuentra solamente en la mitad de los exámenes coprológicos en pacientes con giardiasis; en la otra mitad la aspiración del duodeno es necesaria para confirmar el diagnóstico.

Las pruebas de química de sangre, como son el potasio, sodio, bicarbonato y urea, son necesarias para caracterizar el tipo de deshidratación como hipotónica (sodio menos de 130 miliequivalentes por litro); isotónica (sodio entre 130 y 145 miliequivalentes por litro); o hipertónica (sodio de más de 145 meq/l). El conocimiento de los electrolitos ayuda en el plan de terapia endovenosa para el paciente hospitalizado (6). La gravedad específica de la orina es de gran ayuda para

determinar si la terapia de líquidos es adecuada. El cultivo de orina puede ser de ayuda cuando el cuadro de diarrea no específica se presenta como síntoma principal de una infección urinaria en infantes y en una situación menos común cuando la gastroenteritis causada por *Salmonella* se complica por bacteremia.

#### Manejo:

El manejo general y la terapia antimicrobiana debe ser dirigida al agente etiológico que usted considera sea el más probable, una vez usted ha considerado el historial, los hallazgos físicos y los exámenes de laboratorio rutinarios y sencillos. La tabla II ayuda en esta dirección (5). El paciente que no está hospitalizado puede usualmente manejarse con un corto período de ayuna seguido por líquidos claros por 24 a 48 horas y subsiguientemente comenzar gradualmente la dieta usual. Los líquidos claros deben de contener electrolitos y glucosa. En infantes que son propensos a deshidratación hipertónica, la composición electrolítica debe ser baja y se puede conseguir preparaciones comerciales tales como (Pediate<sup>®</sup> o Litren<sup>®</sup>). La leche desnatada hervida no debe de usarse ya que al hervirla, el agua se evapora y concentra los electrolitos a un grado peligroso. Debe de evitarse el uso de sucrosa y lactosa, ya que pueden inducir diarrea osmótica en los casos donde hay una deficiencia de disacaridasa secundaria a la enfermedad diarreica aguda. Refrescos, té con miel y soluciones propietarias son aceptables como líquidos claros.

El uso de antiespasmódicos tales como paregórico (Tintura de opio alcanforada) y Lomotil<sup>®</sup> pueden ofrecer algún alivio de los retortijones y en la diarrea explosiva del intestino delgado, pero tienen la desventaja de disminuir el tiempo de tránsito y por consiguiente aumentar la interacción entre el agente y/o la toxina que está causando la enfermedad y la mucosa del intestino. Estos medicamentos, según se ha demostrado, aumentan la severidad y duración de shigelosis en humanos (7). Este último hecho en adición a la sobredosis frecuente y reacciones idiosincráticas indican que estos medicamentos no tienen lugar en el manejo de la diarrea de infantes y niños y muy pocas indicaciones, si alguna, en pacientes mayores. Estos agentes disminuyen la frecuencia de deposiciones interfiriendo con la motilidad intestinal pero no disminuyen la pérdida de líquidos, enmascaran la deshidratación y pueden prolongar la duración de la enfermedad. Las indicaciones para el uso de antibió-



ticos en el manejo de diarreas infecciosas agudas son limitadas y bien específicas (Véase Tablas II y IV). En solo tres de las enfermedades del intestino delgado se ha probado que los antibióticos son de beneficio. La diarrea provocada por *Escherichia coli* enteropatógena clásica debe ser tratada con Neomicina, 50-100 mg/kg/día en 4 dosis o Colistimetato (Coly-Mycin®) 15 mg/kg/día en 4 dosis. Tetraciclina oral o por sonda nasogástrica es la mejor droga para la erradicación de *Vibrio cholerae* de la excreta. *Giardia lamblia* puede ser tratada con un curso de 5 a 10 días de Quinacrina (Atabrine®), 100 mg tres veces al día por boca o Metronidazole (Flagyl®), 750 mg por boca tres veces al día. Ocasionalmente los síntomas recurren y se requiere un segundo curso de terapia con una droga alterna. Debemos mencionar que en animales experimentales, el uso de Flagyl® se ha asociado a neoplasia.

En la categoría de intestino grueso el número de agentes etiológicos que se puede tratar con agentes antimicrobianos es mayor, pero la elección de la droga depende en la identificación específica del patógeno. Se ha demostrado en una serie de investigaciones con pacientes pediátricos que la resolución de síntomas, signos y de cura bacteriológica de shigelosis puede ser acelerada por un curso de 5 días de antibióticos orales que se absorben por vía intestinal o antibióticos parenterales a los cuales el organismo etiológico sea susceptible *in vitro*. Los fallos clínicos usando drogas que no se absorben tales como neomicina y garamicina a pesar de que el organismo sea susceptible *in vitro*, demuestran que debe de obtenerse un nivel terapéutico en suero sanguíneo y en tejido en vez de un nivel terapéutico intraluminal. Las cepas multiresistentes están aumentando en prevalencia (8). Estas cepas resistentes pueden ser tratadas durante 5 días con ácido nalidíxico (Negram®), 1 gr por boca cada 6 horas o trimetropin-sulfametozazol (Bactrim®, Septra®), 2 tabletas, dos o cuatro veces al día. Un estudio reciente ha demostrado la eficacia de estas últimas drogas (9). Debe de obtenerse consentimiento escrito antes de su uso, ya que la Administración Federal de Drogas no los ha aprobado para este uso.

Varios estudios han demostrado que el curso clínico de gastroenteritis causada por *Salmonella* en el huésped normal no se afecta favorablemente por terapia de antibióticos. En el caso de niños pequeños que tienen la tendencia a tener una enfermedad prolongada y en los pacientes inmunosuprimidos o comprometidos inmunológicamente, que tienen un aumento en el riesgo

de diseminación sistémica, el uso durante 5 a 7 días de antibióticos tales como ampicilina, amoxicilina o cloranfenicol a los cuales el organismo sea susceptible está indicado. El uso rutinario de antibióticos en el tratamiento de gastroenteritis causada por *Salmonella* en el paciente normal está contraindicado ya que se ha demostrado que los antibióticos aumentan el número de portadores y prolongan la enfermedad.

La enterocolitis causada por estafilococos es una emergencia que debe de ser tratada, descontinuando los agentes antimicrobianos de amplio espectro y comenzando inmediatamente la terapia parenteral antiestafilocócica con meticilina o cefalotina, además de vancomicina por boca. El tratamiento óptimo de amibiasis invasiva siempre ha estado bajo disputa. Kean resume el dilema en un comentario recientemente publicado en JAMA (10). El recomienda emetina, cloroquina, metronidazole o quinacrina solo o en combinación para las formas severas que presentan una amenaza a la vida del paciente. Para amibiasis intestinal leve, Metronidazole puede usarse.

En resumen, las medidas dietéticas y de cuidado general deben de ser suficientes para controlar un episodio de diarrea en 24 a 48 horas; no debe de usarse antibióticos hasta que el cultivo de excreta nos revele el organismo etiológico o hasta que haya una señal clínica específica que indique el patógeno, al cual un antibiótico pueda ser específicamente dirigido. Pruebas de sensibilidad deben de hacerse rutinariamente para poder dirigir la terapia específica al organismo envuelto.

## Referencias

1. Gots, R., Formal, S., Giannella, R.: Indomethacin inhibition of salmonella typhimurium, shigella flexneri and cholera-mediated rabbit ileal secretion. J Infect Dis 130 (3): 280-284, 1974.
2. Sack, R., et al: Enterotoxigenic escherichia coli-associated diarrheal diseases in Apache children. N Engl J Med 292 (20): 1041-1045, 1975.
3. DuPont, H., et al: Pathogenesis of escherichia coli diarrhea. N Engl J Med 285 (1): 1-9, 1971.
4. Harris, J., DuPont, H. and Hornick, R.: Fecal leukocytes in diarrhea illness. Ann Intern Med 76 (5): 697-703, 1972.
5. Davidson, G., et al: Importance of a new virus in acute sporadic enteritis in children. Lancet 1: 242-245, 1975.
6. Finberg, G.: Dehydration secondary to diarrhea, in the critically ill child. Philadelphia, WB Saunders Co., 208-219, 1972, Chap 18.

7. *DuPont, H., Hornick, R.:* Adverse effect of Lomotil® therapy in shigellosis. *JAMA* 226 (13): 1525-1528, 1973.
8. *Neu, H., et al:* Antimicrobial resistance of shigella isolated in New York City in 1973. *Antimicrob Agents Chemother* 7 (16): 833-835, 1975.
9. *Nelson, J.:* Trimethoprim-sulfamethoxazole treatment of shigellosis. Abstract No. 114, 15th ICAAC, 1975.
10. *Kean, B. H.:* The treatment of amebiasis: A recurrent agony. *JAMA* 235 (5): 501, 1976.

El tema de esta conferencia, “Rehabilitación—Filosofía, Alcance y Campo de Acción”, está en armonía con los tiempos que corren. Sin embargo, la medicina física es tan vieja como el arte de curar, y la rehabilitación, la restauración para recobrar la capacidad de ser útil a sí mismo, ha sido anhelada desde que apareció el primer lesionado sobre la faz de la tierra.

La misma razón que obstaculizó el desarrollo de la rehabilitación en los comienzos de la civilización es la que prevalece en la época moderna: el hecho de que en muchas comunidades no se considera que es económicamente práctico investigar los beneficios del programa que vamos a discurrir en estos próximos días.

En el pasado, esta falacia se prestó para que se estableciera un aura alrededor de los lisiados: primero, de mal agüero; luego, de bondad a medida que tomaban auge las creencias religiosas. Las razas guerreras, obedeciendo el criterio de la supervivencia del más fuerte, sacrificaban a los lisiados y a los ancianos. Estas naciones, que vivían por la espada, perecieron todas por la espada. A medida que fue floreciendo el cristianismo, las enseñanzas de la “Regla de Oro” fueron surgiendo gradualmente del alma humana. Antes del Siglo XX, sin embargo, las prácticas de la rehabilitación eran, cuando más, una lucha personal en la que sólo alcanzaban éxito los más perseverantes, y la muerte segaba el mayor número de lisiados a temprana edad.

Actualmente la ciencia está alargando la vida humana, y los genios de la invención están perfeccionando

máquinas y otros artefactos que apenas requieren esfuerzo físico para reproducir los movimientos humanos que se requieran. Esto compensa la destrucción de cuerpo y mentes humanas mediante los múltiples episodios de guerras frías y calientes prevalecientes en esta generación. Dijérase que la rehabilitación es el logro natural de este siglo para compensar el terrible pecado, repetido y aparentemente sin fin, de la matanza humana. Todas las guerras tienen su razón económica; igualmente la tiene la batalla contra las enfermedades y las lesiones que incapacitan. Podedis estar seguros de que el resurgimiento que ha tenido la importancia de la rehabilitación se basa en la dura verdad de que una rehabilitación fructífera significa dinero contante y sonante. No es solamente una demostración de fervoroso amor fraternal del hombre hacia sus semejantes.

El concepto filantrópico de la “Mano que viene en nuestra ayuda”, tan íntimamente entrelazado en el caso de los lesionados, fue y en gran parte es todavía, la columna vertebral de la práctica de la medicina de la rehabilitación en casi todos los países del mundo. Miles de niños y adultos lisiados han reducido hasta el mínimo su incapacidad y han regresado a sus empleos gracias a los hábiles métodos de estos centros privados de rehabilitación. En cada país hay un magnífico centro de rehabilitación como ejemplo vivo y verdadero de este concepto, gracias al espíritu filantrópico y labor incesante del cuerpo profesional y en especial, los distinguidos desinteresados voluntarios.

El estudio del hombre, sus emociones y sus enfermedades continuará mientras exista un solo espécimen humano. La lucha eterna para hacer una mejor especie de “Homo Sapiens” es la razón para reunimos hoy en la Décimo-Tercera Asamblea Mundial de Rehabilitación Internacional en Tel-Aviv, la romántica ciudad de Israel. Todos estamos interesados en preservar la dignidad del hombre y por eso es que nos interesa la medicina de rehabilitación.

El hombre promedio es un animal gregario. Su naturaleza básica lo lleva a vivir en grupo: primariamente

---

*Del Servicio de Medicina de Rehabilitación, Hospital de Veteranos, San Juan, Puerto Rico y Medicina Física y Rehabilitación, Escuela de Medicina, Universidad de Puerto Rico, GPO Box 4867, San Juan, Puerto Rico 00936.*

*Presentada en la Décimo-Tercera Asamblea Mundial de Rehabilitación Internacional en Tel-Aviv, Israel, Junio 13-18, 1976.*



en el seno de su familia, cerca de sus vecinos y su comunidad, con pronto espíritu de servicio para su nación, remotamente interesado en el resto del mundo y vagamente en el universo. No es natural en el hombre, siendo de mente sana, encerrarse fuera de la humanidad aunque fuese la persona más incapacitada físicamente en el mundo. El hombre lucha por ser aceptado como un miembro del grupo. El desea compartir sus responsabilidades y ofrecer su aportación para la preservación de la raza y así confirma su status propio en la comunidad.

Ahora, algunas personas nacen con incapacidades, bien físicas, o mentales o ambas, y otras las adquirieron en el transcurso de sus vidas. Esto no significa que este individuo es un ser inferior por el hecho de que su configuración no conforma dentro de las normas trazadas por la sociedad donde vive. No hay uno solo entre nosotros hoy, que no tenga algún defecto de acuerdo con los conceptos corrientes. Estos no nos hacen inferiores a los demás, ¿no es cierto? Aún podemos funcionar dentro de nuestro medio, ¡y muy bien por cierto! Por otro lado, hay personas cuyo defecto es tan grande que deben ser provistas de los medios con los cuales pueden descubrir y alcanzar la meta que los independiza. Hay a quienes hay que enseñar cómo preservarse mediante su propio esfuerzo o con ayuda de otros más afortunados. Nosotros estamos dedicados a brindarles a estos seres humanos las oportunidades que necesitan en la lucha constante para encontrar una solución satisfactoria.

Según la ciencia médica ha ido conquistando las enfermedades, así también ha multiplicado las complicaciones de la vida. El hombre vive ahora doble la edad de su bisabuelo. Nuestros hospitales se están llenando lentamente de ancianos, pacientes crónicos y niños y adultos incapacitados. El "Staff" médico no se interesa mayormente por el paciente con un diagnóstico tan poco brillante como hemiplegia, artritis degenerativa, o perlesía cerebral. La admisión de un caso de mielitis transversa con su resultante paraplegia trae a la mente del médico residente la inevitable complicación de úlceras de decúbito y muerte como una bendición secundaria a fallo renal después de un período de hospitalización prolongado ocupando una cama necesaria para otros ingresos. Hoy en día que aumenta la longevidad, el hospital para enfermedades agudas es mal llamado. Un cuarenta por ciento de las camas de nuestros hospitales generales están ocupadas por ancianos, enfermos crónicos, y niños y adultos incapacitados. Es precisamente para el tratamiento de este creciente tipo de pacientes que es necesario un pro-

grama efectivo de medicina física y rehabilitación en cada hospital general. Este gran grupo de pacientes requiere cuidado individual por un período más prolongado que cualquier otro y el costo de hospitalización es escalofriante.

Si son devueltos sin tratamiento a su hogar, el costo al gobierno en términos de bienestar público, en ahorros de la familia y el tiempo invertido en cuidarlos es fantástico. Cuanto mejor sería para todos si se les brindase la oportunidad de regresar a una vida productiva o por lo menos una autosuficiente, social y económicamente. Ningún miembro del personal médico del hospital, una vez se le hayan explicado claramente los beneficios de rehabilitación, podría negar esta necesidad. Ningún estado, una vez entienda la economía en dinero y brazos, podría negarse a beneficiarse de la organización de un centro completo de rehabilitación.

Un programa de esta naturaleza dentro de un hospital general debe incluir un servicio de medicina física y rehabilitación y una sala o varias camas para rehabilitación. No es suficiente que los pacientes sean referidos para tratamiento con alguna modalidad física. Debe haber una sala de rehabilitación a donde el médico y el cirujano puedan referir o trasladar sus pacientes como preparativo para alta de hospital una vez terminado su tratamiento. Al removerse estos pacientes de las salas de casos agudos, le permite al personal médico dedicar todo su tiempo a aquellos casos que más lo requieran sin tener que ocuparse de largas convalecencias, pacientes crónicos, ancianos, o incapacitados. Esta clase de programa significa la continuidad del excelente cuidado moderno a través de las tres etapas de medicina: diagnóstico, tratamiento definitivo y rehabilitación o el retorno del paciente a su hogar y su comunidad en el mejor estado físico, mental, social, y económico posible.

La medicina física y rehabilitación ofrece las formas o instrumentos para tratamiento más antiguos conocidos en la medicina. Sin embargo, ofrece la manera más sistemática de un tratamiento completo. Además reduce materialmente los costos de funcionamiento del hospital y los pacientes en la casa.

El principal propósito de una sala de rehabilitación es salvar los aparentemente improductivos miembros de la población. Estos caen en tres categorías:

1. Aquellos parcialmente limitados que pueden trabajar parte del tiempo o hacer trabajo limitado.
2. Aquellos que no pueden trabajar en alguna forma pero que pueden cuidarse a sí mismos.
3. Aquellos que no pueden siquiera cuidarse de sí mismos por completo y necesitan ayuda para ello,

particularmente en la alimentación y la higiene personal.

Como la medicina y la cirugía no han encontrado la cura para muchas de las condiciones lisiantes que producen las categorías arriba mencionadas, estos pacientes son usualmente abandonados a su destino. Muchos en estas categorías pueden ser rehabilitados y retornados a una vida más útil y productiva. Muchos en el primer grupo pueden hacerse más productivos. Muchos en el segundo pueden entrenarse para trabajo parcial o liviano. Finalmente, muchos en el tercer grupo pueden enseñarse a hacer las actividades funcionales del diario vivir librando miembros de la familia y otros para emplearse gananciosamente.

No es el propósito de este trabajo entrar en los detalles sobre el personal y el equipo necesario para desarrollar este programa. Esto será hecho por otros participantes en estas jornadas más adelante. El mensaje enfatizado es el hecho de que un programa médico se puede utilizar para enlazar de este grupo de pacientes por tanto tiempo olvidado.

El fisiatra debe ser consultado en la misma forma que el cirujano ortopédico, el neurólogo, el pediatra, o cualquier otro especialista, ya que es un experto en su campo, la tercera fase de la medicina. El debe tener absoluto control de los pacientes que son referidos a su sala. El debe seleccionar aquellos que pueden rehabilitarse en algunas de las categorías mencionadas. El no debe permitir que sus camas estén ocupadas indefinidamente por pacientes muy deteriorados mentalmente con los cuales no se puede establecer "rapport". La sala de rehabilitación no debe ser un depósito de los casos terminales y todos aquellos casos para los cuales no hay esperanzas ni posibilidades de ofrecerles alguna medida de rehabilitación.

El paciente en la sala de rehabilitación debe creer que algo tangible y práctico se está haciendo por él. Debe entender la labor de entrenarse para hacer las actividades funcionales del diario vivir. Según vaya progresando con éxito en las tareas de comer, ambular, y de higiene personal se llenará con la satisfacción de acercarse a la meta de la suficiencia personal. Muchos pacientes necesitan aparatos o utensilios especiales para alcanzar este fin.

Antes de que el paciente abandone el hospital, tanto la familia como él deben ser entrevistados por la trabajadora del servicio social. Es tiempo y dinero perdido, por ejemplo, darle una silla de ruedas al paciente si no la puede usar en su casa. La familia también debe venir al hospital para entrenarse en la forma como

puede ayudarlo. Especialmente en pacientes poco motivados o vagos. Este tipo de pacientes puede encontrar a alguien que le haga todas sus necesidades y pedirá que lo den de alta porque no quiere pasar el trabajo de rehabilitarse.

En general, agrupar pacientes incapacitados es psicológicamente efectivo al estimularlos a una mayor actividad. Siempre existe el espíritu de cooperación entre ellos, y los menos limitados ayudan a los más. El paciente sabe que el ser trasladado a la sala de rehabilitación es la etapa final de su estadía en el hospital y concentrará más para sacar el máximo beneficio de su entrenamiento. Algunos inventan métodos y equipos para ayudarse a sí mismos y a otros amigos más desafortunados para vencer sus incapacidades. Hasta preparan a la familia para que los acepten sin reservas al regresar al hogar.

En la sección de terapia ocupacional el paciente aprende artes y oficios que lo pueden ayudar a ganarse la vida. Muchos de nuestros pacientes ganan más dinero hoy de las tareas que aprendieron que antes de incapacitarse. Si su comunidad tiene alguna agencia pública o privada para fomentar el empleo de lisiados, ellos pueden desarrollar habilidades en un programa prevocacional.

Básicamente, medicina física y rehabilitación provee un programa de servicio médico al personal médico del hospital. El servicio incluye diagnóstico, evaluaciones, y tratamientos especiales. Hace uso de equipo especializado y de la forma grupal de tratamiento, la cual es extraña para muchos médicos. El costo de un servicio completo de medicina física y rehabilitación es alto y requiere mucho espacio, el cual no está disponible en muchos de los hospitales más viejos. Por otro lado, el valor socio-económico de este programa ha sido tan conclusivamente demostrado en Puerto Rico que todos los hospitales nuevos y casi todos los viejos proveen este servicio.

Antes de terminar, me gustaría mencionar algunos de los procedimientos de diagnóstico con que el fisiatra puede ayudar a sus colegas para obtener un diagnóstico más correcto y exacto:

1. Evaluación de la fuerza muscular en enfermedades neuromusculares.
2. Estudio sobre el alcance de movimientos de las coyunturas en condiciones musculoesqueletales.
3. Palpación y estimulación eléctrica de músculos en síndromes miofaciales.
4. Métodos de electrodiagnóstico: estimulación eléctrica, cronaximetría, y curvas de duración de fuer-



za para determinar la reacción de degeneración de nervios periféricos; y electromiografía para determinar el estado de los nervios y músculos de las unidades motrices inferiores.

5. El uso de oscilometría y pirometría, en el diagnóstico de enfermedades vasculares obliterantes.
6. La más importante evaluación funcional de los severamente incapacitados, los crónicamente enfermos, y los pacientes ancianos mediante la investigación de sus habilidades para aprender las actividades funcionales de la vida diaria, especialmente del cuidado personal.

El tiempo no me permite discutir en detalle la prevención por medio de medidas físicas de incapacidades superimpuestas, especialmente los efectos lisantes de los cambios degenerativos en las coyunturas y los músculos como resultado de un descanso prolongado en cama. Ambulación temprana, siempre que se puede, después de intervenciones quirúrgicas es el mejor tratamiento. ¿Pero, qué de la prevención de complicaciones circulatorias así como musculoesqueléticas ocasionadas por desuso o mala posición en el paciente que no puede caminar?

Quizás la complicación más seria que sigue a trauma es la atrofia por desuso y la contracción de tejidos blandos como resultado directo o secundario a inmovilización en mala posición funcional. En muchos pacientes esta deformidad es la sola causa de su incapacidad después que la lesión original ha sanado. No es suficiente con decirle al paciente que mueva sus coyunturas, que respire profundamente, y que se mueva con frecuencia en la cama. Hay que tomar tiempo para instruir al paciente en un programa correcto y completo de ejercicios. Estos ejercicios deben ser hechos repetidamente todos los días, y es el médico y el cirujano ocupado quienes tienen que hacer tiempo para ver que el paciente se ejercite. Son estas las deformidades que pueden ser evitadas o minimizadas con un programa activo de medicina física.

Es obvio que el rol de medicina física y rehabilitación en un hospital general es enorme. Hay escasamente

alguna condición patológica que no pueda beneficiarse en alguna forma de una consulta con el fisiatra. La buena práctica de la medicina incluye un bien equipado servicio de medicina física y rehabilitación con un personal bien preparado. A su debido tiempo este programa puede empezar a entrenar personal de rehabilitación para otros hospitales y, finalmente, expandir su enseñanza hacia la investigación.

Estas son, en breves palabras, en una síntesis brevísima, la filosofía, alcance y campo de acción de la rehabilitación. El concepto fisiátrico de un total cuidado médico fue el primer paso para que el paciente fuese visto y tratado no como un sistema específico o un patrón de enfermedad, sino como un completo ser humano. Esta filosofía del total cuidado médico trajo consigo el desarrollo del trabajo en equipo, usando las habilidades especializadas de médicos y personal auxiliar médico. El desarrollo de la especialidad de medicina física y rehabilitación es historia muy moderna, que ha comenzado y sucedido en la vida real de casi todos ustedes presentes.

El cuidado médico no está completo hasta que el paciente haya sido entrenado para vivir y trabajar con lo que le queda. Lo mismo que la ciencia médica está añadiendo años a la vida hoy, así también nosotros debemos añadir vida a los años. En pocas palabras, ésta es la verdadera filosofía de la medicina física y rehabilitación.

Esto sí es una filosofía que ha avanzado al mismo ritmo astronáutico del Siglo XX. La segunda mitad de este siglo ha venido acompañada del descubrimiento de las milagrosas drogas de la década de los Cuarenta, y esta revolución química ha salvado a millares de vidas de la enfermedad. Aún no hay ningún milagro divino que pueda reponer los cuerpos rotos, las mentes enturbiadas, o frenar la desintegración de la vida misma. Pero aunque se ha logrado mucho en la práctica de la medicina física y rehabilitación en el mundo entero, aún se puede y se debe hacer mucho, muchísimo más. Afortunadamente, una vez trillado el camino, es más fácil encontrar la senda.



## *MANY WOMEN ABANDON PILL FOR OTHER CONTRACEPTIVES.*

CHICAGO — Adverse publicity about oral contraception in recent years may be leading to a striking movement away from the pill and back to either mechanical barrier methods or no protection at all against pregnancy, says a research report in the Feb. 7 Journal of the American Medical Association.

A study of 100 women patients at the outpatient unit of the University of California at San Francisco Medical Center revealed that 53 percent of the women had changed contraception methods in the last two years, most commonly moving away from oral contraception, the report says.

Sixteen of the women in the study said they were using no contraception. One woman relied on the rhythm method, and 24 used a mechanical barrier (diaphragm, foam, or condom). Only 28 women were using oral contraceptives, while 16 had an intrauterine device in place. Eight relied on sterilization. Fourteen of the women were dissatisfied with their current method of contraception, usually because of possible hazardous side effects.

The study sought to determine current attitudes toward reproductive and sexual roles. Major areas of change apparent in the younger population were a substantial decrease in formal marriage, a reduction in the wish for children, a movement away from oral contraception and back to mechanical barrier methods, and a shift toward acceptance of a bisexual adaptation, report Susan Wall, RN, and Nancy Kaltreider, MD.

The patients were interviewed by a woman medical student who previously had been a psychiatric nurse, on the premise that women would talk more candidly with a woman than with a male physician. Age range of subjects was from 19 to 75 years, with a median age of 27.9.

A high percentage of nonmarital cohabitation (23 percent) and single living (17 percent) marks a new adherence to alternate life-styles, they report. Some 37 percent of heterosexual women said they considered a homosexual relationship to be a future possibility.

in the chest work very well in prolonging useful life. A majority of the patients survive for a number of years with the pacemakers, and death almost always is caused by an ailment not related to pacemaker failure.

These are the findings of a survey of more than 12 years of experience with the pacemakers at the University of Virginia School of Medicine, Charlottesville, Va., reported in the Feb. 7 Journal of the American Medical Association.

Of the 313 patients who received heart pacemakers between 1961 and 1973, there was a survival rate of 65 percent after five years. Average age at onset of pacing was in the late 60s.

Of the 109 individuals in the study who died, only one death could be attributed directly to failure of the implanted device. The others died from a variety of causes not related to the pacemaker, says Lockart M. McGuire, M. D., and colleagues.

Death rates increased during the later years of the study, primarily because the criteria for selecting implant recipients was broadened considerably to include individuals who were considered poor risks in the earlier years, Dr. McGuire says.

But, he points out, "The benefits of cardiac pacing for even a brief period of two or three years may be highly desirable.

Recent technical innovations have improved the effectiveness of the pacemaker, particularly to extend the life of the power source to four or more years. In the earlier devices, replacement of the power source was necessary at more frequent intervals. Some now use nuclear power.

---

## *ZINC TABLETS FOUND HELPFUL IN CONTROLLING ACNE*

CHICAGO — Tablets of zinc are effective in controlling acne, a Swedish research group reports in the January issue of Archives of Dermatology, a scientific journal of the American Medical Association.

Gerd Michaelsson, M. D., of Uppsala University, Sweden, and colleagues gave their patients three tablets daily of zinc sulfate in effervescent form. The tablets were dissolved in water and taken after meals three times daily.

After four weeks there was a significant decrease in the number of blackheads, whiteheads and pimples. After 12 weeks, the acne had been reduced by 85 percent in those treated, Dr. Michaelsson reports.

---

## *HEART PACEMAKERS EFFECTIVE IN PROLONGING LIFE*

CHICAGO — The heart pacemakers that are implanted

$\frac{20}{150}$

# H

$\frac{20}{100}$

# EAR

$\frac{20}{70}$

# ING IS

$\frac{20}{50}$

# AS PRECIOUS

$\frac{20}{40}$

# AS SIGHT HAVE

$\frac{20}{30}$

# YOU HAD YOUR HEARING

Hearing losses are among the most consistently neglected health problems. Many

$\frac{20}{20}$

# TESTED LATELY A SIMPLE

people with them won't even admit it to themselves, let alone others. A little encouragement may start them thinking about themselves

$\frac{20}{15}$

# COMFORTABLE HEARING

more realistically.

$\frac{20}{10}$

# INVESTMENT OF A FEW MINUTES

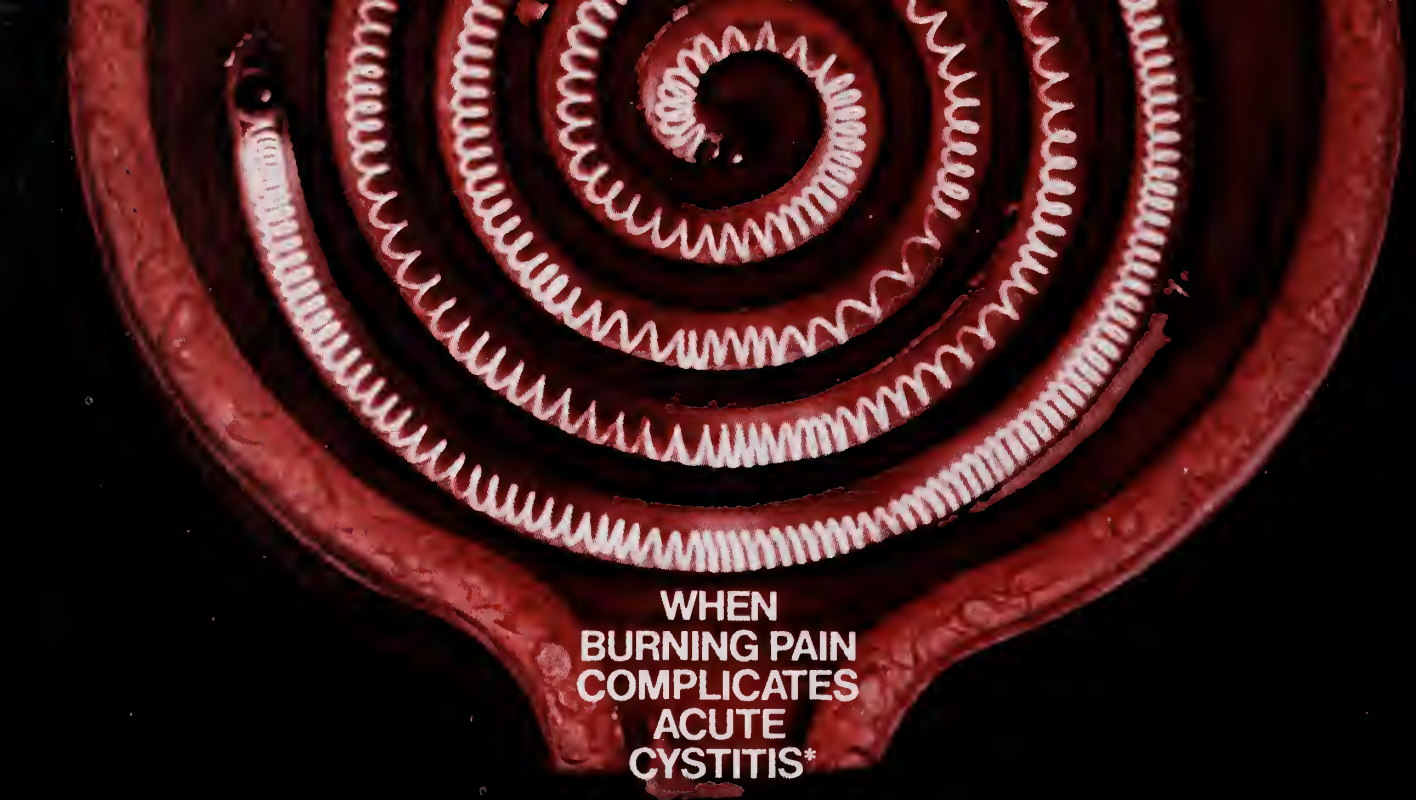
That's why we're offering you the poster shown here. You can hang it on the wall or stand it on a small table. It comes with booklets called "As precious as sight" that give your patients some basic facts about auditory testing and hearing losses and how easy they are to correct in many cases.

Write to us for your free poster and booklets. They just might help you to help some patients who aren't hearing as well as they used to. Even those who ordinarily wouldn't hear of it.

Professional Relations Division, Beltone Electronics Corporation  
4201 West Victoria Street, Chicago, Illinois 60646, an American company

***Beltone***  
WHEN A HEARING  
AID WILL HELP





WHEN  
BURNING PAIN  
COMPLICATES  
ACUTE  
CYSTITIS\*

TURN IT OFF WITH

# AZO GANTANOL<sup>®</sup>

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

## FOR THE PAIN

- Quickly relieves painful symptoms such as burning and pain associated with urgency and frequency.
- Recommended antibacterial therapy: up to 3 days with Azo Gantanol, then 11 days with Gantanol (sulfamethoxazole).

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies.

**Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura,

## FOR THE PATHOGENS

- Effectively controls susceptible pathogens such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

\*nonobstructed; due to susceptible organisms

hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

**Dosage:** Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**NOTE:** Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



# DYAZIDE®

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

Trademark

## MAKES SENSE FOR LONG-TERM CONTROL OF HYPERTENSION\*



Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### WARNING

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**Indications:** When the fixed combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium-sparing action of its 'Dyrenium' component is warranted.

**Contraindications:** Further use in progressive renal or hepatic dysfunction; hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs. Routine use of diuretics in otherwise healthy pregnancy.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with

cardiac irregularities. It is more likely in severely ill patients with urine volume less than one liter/day, the elderly or diabetics, with suspected or confirmed renal insufficiency. Periodic determinations of serum  $K^+$  should be made. If hyperkalemia develops, substitute a thiazide alone, restrict  $K^+$  intake. The presence of a widened QRS complex or arrhythmia in association with hyperkalemia requires prompt additional therapy. Thiazides are reported to cross the placental barrier and appear in breast milk; fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and other adverse reactions that have occurred in the adult may result. When used in pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics, or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spiro-lactone is used concomitantly, determine serum  $K^+$  frequently; both can cause  $K^+$  retention and elevated serum  $K^+$ . Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium® (triamterene, SK&F Co.), and

leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Do periodic blood studies in cirrhotics to check for nondrug-related variations in blood pictures, and in patients with folic acid depletion, since 'Dyrenium' may contribute to appearance of megaloblastosis. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

**Adverse Reactions:** Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

**Supplied:** Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

**SK&F CO.,** Carolina, P.R. 00630  
Subsidiary of SmithKline Corporation

## TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE


## A N U N C I O

Magnífico local para oficina de médico o dentista localizado en la Calle Máximo Alomar Núm. 1167, (Esquina) Urbanización San Agustín, Río Piedras, Puerto Rico (entre Centro Comercial 65 de Infantería y Escuela Superior República de Colombia). Este local tiene 594 pies cuadrados y está listo para ocuparse. Renta mensual \$375.00 — Para información, teléfonos 763-2575 y 763-0385.

## WANTED

Family practitioner and/or internist-cardiologist by six men multi-specialty group in Mid-East Tennessee. Town of 7,000 with a drawing area of 60,000 population. Modern Clinic Building adjacent to ultra-modern 200 bed Medical Center. No investment. First year guaranteed ample salary plus multiple fringe benefits. Must be able to obtain a Tennessee Medical License and speak English fluently. Ideal situation for a U. S. or P. R. trained physician wishing to relocate in U. S. If interested, contact: Ramón Sánchez Viñas, M. D. , Cumberland Clinic, 301 Hayes Street, Crossville, Tennessee, 38555, (615) 484-5171.





**"Little Boy Blue,  
come blow your horn,  
The sheep's in the  
meadow, the cow's  
in the corn..."**

Since cow's milk and corn are leading causes of food allergy among infants, NEO-MULL-SOY® formula doesn't contain either one. Other leading soy formulas do contain corn syrup. Next time recommend corn-free NEO-MULL-SOY formula first. Mothers like its milky whiteness. And now it's easier for them to find NEO-MULL-SOY formula, because it's more readily available at grocery and drug stores.



**NEO-MULL-SOY®**

Soy Isolate Formula

**The only leading soy formula  
that's milk-free AND corn-free.**

**SYNTEX**

SYNTEX LABORATORIES, INC.  
PALO ALTO, CALIFORNIA 94304



# Septra® vs Nitrofurantoin

Each tablet contains:  
80 mg trimethoprim and 400 mg sulfamethoxazole

## A new clinical

### **Efficacy: A draw.**

By randomized assignment, 149 patients received two Septra tablets b.i.d. and 140 received one 100 mg capsule of nitrofurantoin macrocrystals q.i.d. for 14 days. Eight days after therapy ended, 94% of patients treated with Septra had a clear culture vs 90% of those treated with nitrofurantoin macrocrystals.<sup>1</sup>

### **Laboratory changes: A draw.**

There was no significant difference in the incidence of laboratory changes except in one instance; a significantly larger proportion of patients on nitrofurantoin macrocrystals had decreased lymphocyte counts than did patients on Septra.<sup>1</sup> The significance of this change is not known. (For further details see page three of this advertisement.)

### **Clinical side effects: Advantage, Septra.**

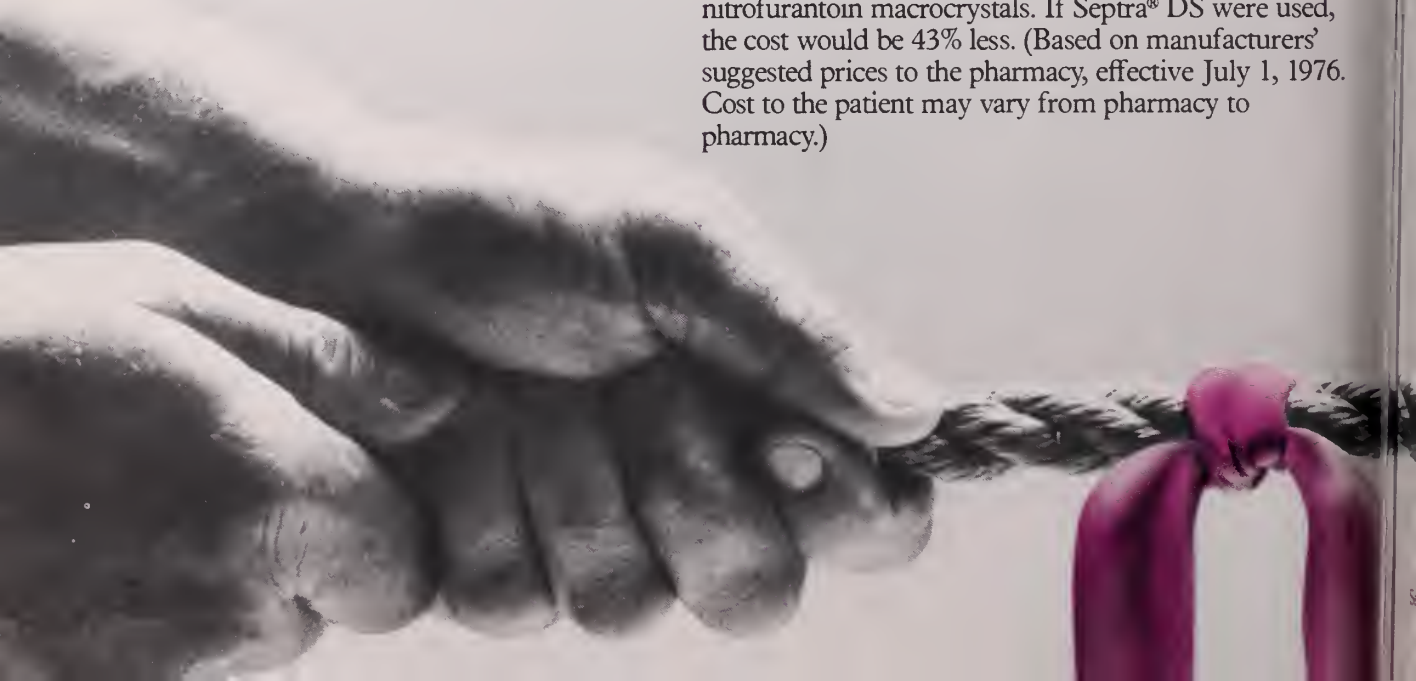
A significantly larger proportion of patients experienced side effects on nitrofurantoin macrocrystals (13%) than on Septra (6%).<sup>1</sup> (For further details, see chart on page three of this advertisement.)

### **Convenience: Advantage, Septra.**

To maintain effective antibacterial activity, Septra is taken just twice a day, while nitrofurantoin macrocrystals are taken four times daily. The Septra dosage schedule offers obvious advantages in terms of patient convenience and compliance.

### **Cost: Advantage, Septra.**

At the dosages used in this study, a course of therapy with Septra would cost 26% less than a course of nitrofurantoin macrocrystals. If Septra® DS were used, the cost would be 43% less. (Based on manufacturers' suggested prices to the pharmacy, effective July 1, 1976. Cost to the patient may vary from pharmacy to pharmacy.)



# nitrofurantoin

Macrocrystals

## confrontation

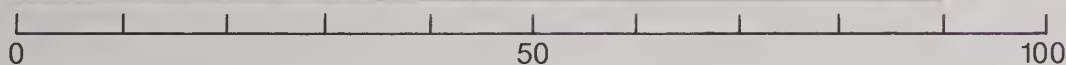
Results after 14-day course of therapy in 289 patients with recurrent urinary tract infections\*<sup>1</sup>

**Septra**

**94%**

**Nitrofurantoin**  
Macrocrystals

**90%**



% of patients with clear culture 8 days after therapy ended

\*Due to susceptible strains of *E. coli*, *Klebsiella*, *Enterobacter*, *Proteus mirabilis* and other *Proteus* species. Criterion for infection—100,000 or more organisms/ml urine. Criterion for "clear culture"—1,000 or fewer organisms/ml urine.

# Septra<sup>®</sup> DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

**Double Strength Tablets.**

**The most economical form of Septra.**





# Septra<sup>®</sup> vs Nitrofurantoin

Each tablet contains:  
80 mg trimethoprim and  
400 mg sulfamethoxazole

Macrocrystals

## Clinical side effects: Advantage, Septra.

Side effect	Frequency <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
nausea	3	16
vomiting	1	9
anorexia	1	4
abdominal pain	—	2
diarrhea	—	4
headache	2	—
dizziness	—	1
diaphoresis	1	—
pruritus	2	1
vaginitis	1	—
maculopapular rash	1	1
rash	—	2
urticaria	2	—
	14	40

**Note:** All patients who originally entered the study described on previous pages were included in the evaluation for clinical side effects (192 patients received Septra, 191 received nitrofurantoin macrocrystals). Some patients experienced more than one side effect. See **Adverse Reactions** section below for other reactions that may be encountered.

## Laboratory changes: A draw.

Type of change	Drug administered No. patients with change/total patients tested <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
RBC ↓	14/141	14/141
Hemoglobin ↓	27/188	36/183
WBC ↑	3/188	3/183
" ↓	6/188	7/183
Bands ↑	3/183	3/176
" ↓	26/183	20/176
Hematocrit ↓	34/188	27/183
SGOT ↑	5/176	4/167
Basophils ↑	14/179	16/171
Neutrophils ↑	27/188	25/182
" ↓	3/188	6/182
Lymphocytes ↑	15/188	18/182
" ↓	11/188	21/182
Eosinophils ↑	14/179	8/177
Monocytes ↑	10/188	11/180
" ↓	23/188	23/180
Specific gravity ↑	1/187	—
" ↓	—	1/177
Casts ↑	6/186	5/182
WBC/HPF ↑	9/190	13/185
RBC/HBF ↑	12/190	12/185
Bacteria ↑	9/189	11/183
" ↓	30/189	32/183
Crystals ↑	9/185	9/181

**Note:** Certain patients were not tested for some of the laboratory values listed above. Therefore, the chart specifies the total number of patients who completed the prescribed series of tests for each individual laboratory measurement.

**Indications:** Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37: 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. At present, data are insufficient to recommend use in infants and children under 12.

**Precautions:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria,

serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

**Supplied:** Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

**Reference:** 1. Data on file, Medical Department, Burroughs Wellcome Co.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



There is only one  
macrocrystal  
nitrofurantoin...  
and only Eaton  
has it.

Eaton

Consistent  
potency  
against the  
most prevalent  
uropathogens.

# Macrochantin<sup>®</sup> (nitrofurantoin macrocrystals)

capsules 25mg 50mg 100mg



**® EATON LABORATORIES**  
Norwich International  
410 Park Avenue  
New York, N.Y. 10022  
U.S.A.

**INDICATIONS:** Indicated for the treatment of pyelonephritis, pyelitis, and cystitis due to susceptible *E. coli*, enterococci, *S. aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses) and certain strains of *Klebsiella-Aerobacter*, *Proteus* and *Pseudomonas*.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function; infants under one month; pregnant patients at term; known hypersensitivity

**WARNINGS:** May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. (Such patients should be closely observed while receiving nitrofurantoin.) Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to *Pseudomonas*. Safety not established during pregnancy and lactation; should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.

**PRECAUTIONS:** Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal

impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**ADVERSE REACTIONS: Gastrointestinal Reactions**—Anorexia, nausea, emesis are the most frequent reactions; less frequently, abdominal pain and diarrhea, rarely, hepatitis. This dose-related toxicity reaction can be minimized by reduction of dosage, especially in the female patient.

**Hypersensitivity Reactions**—Pulmonary sensitivity reactions, which can be acute, subacute, or chronic. Acute reaction is commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on X-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and resolve with cessation of the drug therapy. Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation

of the drug therapy

**Dermatologic Reactions**—Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other Sensitivity Reactions**—Anaphylaxis, osmotic attack in patients with history of asthma, cholestatic jaundice, drug fever, and orthralgia

**Hematologic Reactions**—Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy

**Neurological Reactions**—Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness

**Miscellaneous Reactions**—Transient alopecia

**SUPPLIED:** Macrochantin (nitrofurantoin macrocrystals) is available in opaque, yellow capsules of 100 mg (coded "Eaton 009") and in opaque, yellow and white capsules of 50 mg (coded "Eaton 008") in bottles of 30, 100, 500, and 1,000 capsules, and in opaque, white capsules of 25 mg (coded "Eaton 007") in bottles of 100 capsules. Macrochantin Capsules, 50 mg and 100 mg, are also available in hospital unit-dose packages, strip-packaged in boxes of 100.

**antifungal**

**antipruritic**

**antibacterial**

**anti-  
inflammatory**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform® hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**Possibly\* effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; lichen planus; chronic eczematoid otitis externa; acne vulgaris; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, or varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Use in Pregnancy

Though topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant women has not been established. Therefore, this drug should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm.

**Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

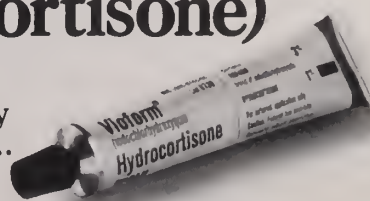
Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/6867 17

# Vioform- Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A



#### Brief Summary

**Indication:** Hypertension. (See box warning.)

**Contraindications:** Mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases

#### Warnings:

This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Use with caution in patients with severe renal disease, impaired hepatic function or progressive liver disease. Regroton may potentiate action of other antihypertensive, ganglionic and peripheral adrenergic-blocking drugs. Sensitivity reactions may occur in allergic and asthmatic patients. Discontinue Regroton one week before electroshock therapy, and if depression or peptic ulcer occurs. **Use in pregnancy:** Thiazides cross the placental barrier and appear in cord blood. The use of chlorthalidone and related drugs in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Use with care in nursing mothers since thiazides and reserpine cross the placental barrier and appear in cord blood and breast milk. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated mothers. If use of the drug is essential, the patient should stop nursing.

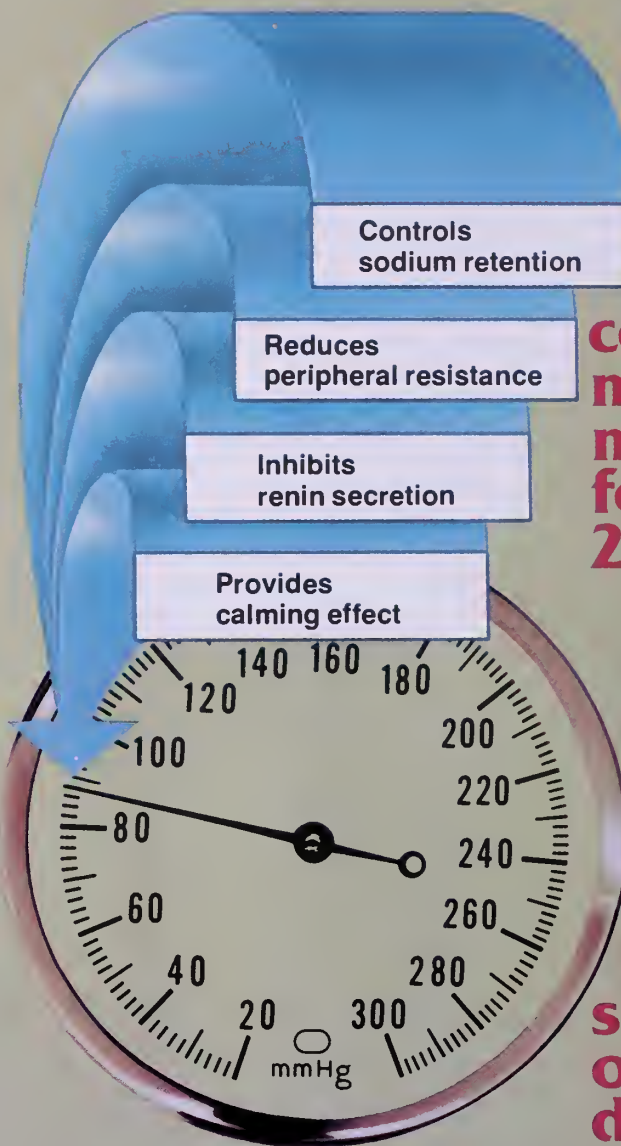
**Precautions:** Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use anticholinergic or adrenergic drugs or other supportive measures if needed. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue Regroton if the BUN rises or liver dysfunction is aggravated (hepatic coma may be precipitated). Patients receiving chlorthalidone should have periodic determination of serum electrolytes and should be observed for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis and hypokalemia), particularly if they are receiving digitalis, parenteral fluids, or are vomiting excessively. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. Use Regroton cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients.

**Adverse Reactions:** The drug is generally well tolerated. The most frequent adverse reactions are anorexia, nausea, vomiting, gastric irritation, diarrhea, constipation, headache, dizziness, weakness, muscle cramps, nasal congestion, drowsiness and mental depression. Other potential side effects include skin rash, urticaria, ecchymosis; hyperglycemia and glycosuria (diabetics should be checked regularly), hyperuricemia and acute gout, and impotence. With chlorthalidone: restlessness, transient myopia; dysuria, orthostatic hypotension (may be potentiated by alcohol, barbiturates or narcotics), rare idiosyncratic reactions such as aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, purpura, necrotizing angitis and Lyell's syndrome (toxic epidermal necrolysis); pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration; other reactions reported with this class of compounds include jaundice, xanthopsia, paresthesia, and photosensitization. With reserpine: angina pectoris, bradycardia, ectopic cardiac rhythms (especially with digitalis); blurred vision, conjunctival injection, uveitis, optic atrophy, glaucoma, deafness, increased gastric secretions, dull sensorium, paradoxical anxiety, nightmares, reversible paralysis agitans syndrome, dyspnea, weight gain, dryness of mouth, increased susceptibility to colds, decreased libido, skin flushing and pruritus. **Dosage:** Should be determined by individual titration. (See box warning.) Dosage for most patients is one tablet once a day.

**How Supplied:** Pink, round, single-scored tablets in bottles of 100 and 1000.

# In moderate to moderately severe hypertension

## Regroton®



Combines two long-acting agents... following titration offers a simple regimen that encourages compliance through convenience and economy.

# Regroton®

Each tablet provides:  
chlorthalidone USP 50 mg., reserpine USP 0.25 mg.

## matches medication to mechanisms

**USV**  
LABORATORIES

USV Laboratories Inc.  
Manati, P.R. 00701

## To relieve nausea and vomiting associated with

- postoperative recovery
- radiation therapy
- chemotherapy
- acute situations

(Contraindicated in pregnancy, severe CNS depression, comatose states and in patients who have demonstrated a hypersensitivity to phenothiazines.)

## Three dosage forms with the same 10 mg dosage strength:

**Tablets**—10 mg (thiethylperazine maleate, NF)



**Suppositories**—10 mg (thiethylperazine maleate, NF)



**Injection**—10 mg/2cc ampul (thiethylperazine maleate, NF) for IM use only.



# Torecan®

(thiethylperazine)

Still available in  
Puerto Rico



**Boehringer Ingelheim**

Boehringer Ingelheim Ltd.  
Elmsford, New York 10523

**Torecan®** (thiethylperazine)

Tablets, Suppositories and Injection

**Contraindications:** Severe CNS depression, comatose states, and in patients who have demonstrated a hypersensitivity to phenothiazines (e.g., blood dyscrasias, jaundice). Because severe hypotension has been reported after the intravenous administration of phenothiazines, this route of administration is contraindicated. The drug is contraindicated in pregnancy.

**Warnings:** Phenothiazines are capable of potentiating CNS depressants as well as atropine and phosphorous insecticides. The drug may impair mental and/or physical ability required in the performance of potentially hazardous tasks such as driving a car or operating machinery.

**Postoperative Nausea and Vomiting:** When used to control postoperative nausea and vomiting in patients undergoing elective surgical procedures, restlessness and postoperative CNS depression during anesthesia recovery may occur. Possible postoperative complications of a severe degree of any of the known reactions of this class of drug must be considered. Postural hypotension may occur after an initial injection, rarely with the tablet or suppository. Do not use with epinephrine in the treatment of drug-induced hypotension as phenothiazines may induce a reversed epinephrine effect. The most suitable vasoconstrictor agents are levaterenol and phenylephrine. The use of Torecan has not been studied following intracardiac and intracranial surgery. Not recommended for use in children under 12 years of age, or in nursing mothers since safety and efficacy have not been established.

**Precautions:** Convulsions and abnormal movements such as extrapyramidal symptoms have occurred. The varied extrapyramidal symptom complex is more likely to occur in young adults and children. Extrapyramidal effects must be treated by reduction of dosage or cessation of medication. For treatment of nausea and/or vomiting associated with anesthesia and surgery, the drug should be administered by deep intramuscular injection at or shortly before the termination of anesthesia.

**Adverse Reactions:** CNS: convulsions, extrapyramidal symptoms such as dystonia, torticollis, oculogyric crisis, akathisia and gait disturbances, occasional cases of dizziness, headache, fever and restlessness have been reported. Drowsiness may occur initially on injection but is usually alleviated by a reduction in dosage. Dryness of the mouth and nose, blurred vision, tinnitus, sialorrhea and altered gustatory sensation. Peripheral edema of the arms, hands and face. Cholestatic jaundice; cerebral vascular spasm and trigeminal neuralgia have been reported occasionally. The following have occurred with phenothiazine derivatives and should be considered: agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia, pancytopenia, eosinophilia, leukocytosis; miosis, obstipation, anorexia, paralytic ileus, erythema, exfoliative dermatitis and contact dermatitis; jaundice, biliary stasis. Hypotension, rarely leading to cardiac arrest, ECG changes. Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonos, oculogyric crises, tremor, muscular rigidity, akinesia, some of which have persisted for several months or years especially in patients of advanced age with brain damage. Menstrual irregularities, altered libido, gynecomastia, weight gain; false positive pregnancy tests. Urinary retention, incontinence; fever, laryngeal edema and angioneurotic edema, asthma. Hyperpyrexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. ECG changes. While there is no evidence that ECG changes are in any way precursors of any significant disturbance of cardiac rhythm, sudden and unexpected deaths apparently due to cardiac arrest have been reported in a few instances in hospitalized psychotic patients previously showing characteristic ECG changes. A peculiar skin-eye syndrome, which is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea, has also been recognized as a side effect following long-term treatment. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported.

**Drug Interactions:** Phenothiazines are capable of potentiating CNS depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorous insecticides. The drug may induce a reversed epinephrine effect on occasion.

For complete details, please see full prescribing information.

LISTA DE ANUNCIANTES

1.	BELTONE ELECTRONICS	HEARING AIDS
2.	BOEHRINGER INGELHEIM	TORECAN
3.	BURROUGHS WELLCOME	CODEINE ANAL., SEPTRA DS
4.	CIBA PHARM.	VIOFORM - HC
5.	EATON LAB.	MACRODANTIN
6.	MERCK SHARP & DOHME	ALDOMET
7.	ROCHE LAB.	AZO GANTANOL, BACTRIM, VALIUM
8.	SYNREX LAB.	NEO-MULL-SOY
9.	UPJOHN CO.	TOLINASE
10.	SMITH, KLINE & FRENCH	DYAZIDE
11.	U. S. V. PHARM.	HYGROTON



PLAY  
LIVES

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

JUN 10 1977



THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET  
BOSTON, MASS. 02115

# A character all its own.



Valium (diazepam) is a benzodiazepine with a character all its own.

Pharmacologically, it has been described as more potent mg-per-mg than other available anxiolytic benzodiazepines. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> (diazepam)<sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



# THREE-IN-ONE THERAPY AGAINST TOPICAL INFECTION

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

JUN 10 1977

## Neosporin<sup>®</sup> Ointment

(Polymyxin B-Bacitracin-Neomycin)

This potent broad-spectrum antibacterial provides overlapping action to help combat infection caused by common susceptible pathogens (including staph and strep). The petrolatum base is gently occlusive, protective and enhances spreading.

### Neomycin

*Staphylococcus*  
*Haemophilus*  
*Klebsiella*  
*Aerobacter*  
*Escherichia*  
*Proteus*  
*Corynebacterium*  
*Streptococcus*  
*Pneumococcus*

### Bacitracin

*Staphylococcus*  
*Corynebacterium*  
*Streptococcus*  
*Pneumococcus*

### Polymyxin B

*Pseudomonas*  
*Haemophilus*  
*Klebsiella*  
*Aerobacter*  
*Escherichia*

*In vitro* overlapping antibacterial action of  
Neosporin<sup>®</sup> Ointment (polymyxin B-bacitracin-neomycin).



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

## Neosporin<sup>®</sup> Ointment

(Polymyxin B-Bacitracin-Neomycin)

Each gram contains: Aerosporin<sup>®</sup> brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs; in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is

affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



## ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial

Fundado en 1903

Volumen 69

Abril 1977

Número 4

## JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bermúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

## Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

## Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

## Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

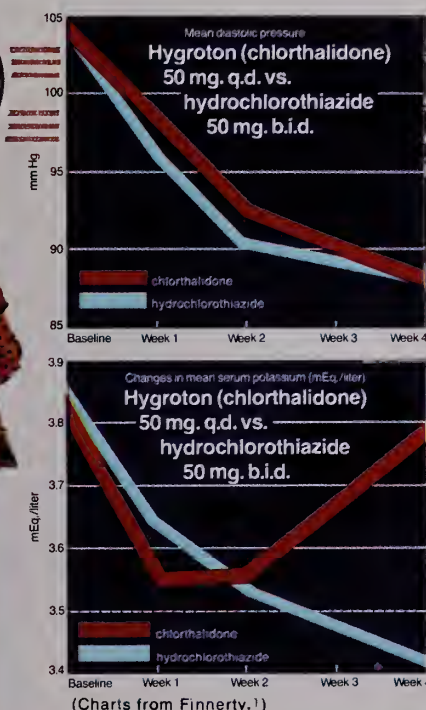
Second Class postage paid at San Juan, P. R.

## CONTENIDO

Hyperlipoproteinemic Types Among Puerto Ricans: A Final Report .....	102
<i>Marta Cancio, Ph D and José M. León, BS, MT</i>	
Factores Socioepidemiológicos del Uso de Drogas Entre los Estudiantes de las Escuelas Secundarias de Puerto Rico .....	113
<i>Rafaela Robles, Ed.D, Ruth Martínez, B.A., Ana I. Colón, B. A., y Margarita Moscoso, B. A.</i>	
The Safety of Percutaneous Arteriography: Indications, Techniques and Results .....	120
<i>R. García Rinaldi, MD, PhD, C. H. McCollum, MD, J. M. Graham, MD, W. W. Defore, MD, and M. E. DeBakey, MD.</i>	
Coronary Artery Aneurysm: Case Report with Review of Literature .....	129
<i>Rafael A. Cox, MD, Pablo I. Altieri, MD, Fernando Martínez Catinchi, MD and Félix I. León Rivero, MD</i>	
Notas Terapéuticas: Las Penicilinas .....	134
<i>Carlos H. Ramírez Ronda, MD, FACP, Carlos León Valiente, MD y Ramón H. Bermúdez, MD</i>	
Carta al Editor : Síndrome de Hipo-neoglucogenia .....	140
<i>Angel Rodríguez Olleros, MD</i>	
Editorial: La Hiperlipemia en Puerto Rico .....	141
<i>José M. Torres, MD, FACP, FACC</i>	
Noticias .....	143

PORTADA: Iglesia San José, Viejo San Juan  
(Cortesía: Dr. Rafael E. Ramírez)

# New double-blind study In hypertension... Hygroton (chlorthalidone) vs. hydrochlorothiazide



## Hygroton achieves

## Goal pressure with single daily doses

"Two 50 mg tablets of hydrochlorothiazide were required to produce the same blood pressure lowering effect as one 50 mg tablet of chlorthalidone..." Frank A. Finnerty, Jr.<sup>1</sup>

## More positive potassium profile

The advantages of chlorthalidone over hydrochlorothiazide "...should be reflected in better patient compliance, because of its... potential for fewer side effects resulting from decreased potassium..."

Frank A. Finnerty, Jr.<sup>1</sup>

# Hygroton® (chlorthalidone) 50 mg. blocks sodium retention longer

### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased

decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg (white, scored) and 50 mg (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6.

**Reference:** 1. Finnerty, F. A., Jr.: Hypertension: The Continuing Challenge, Scientific Exhibit, Meeting of AAFP, Boston, Mass., Sept. 20-23, 1976.

**USV  
LABORATORIES**

USV Laboratories Inc.  
Manati, P.R. 00701

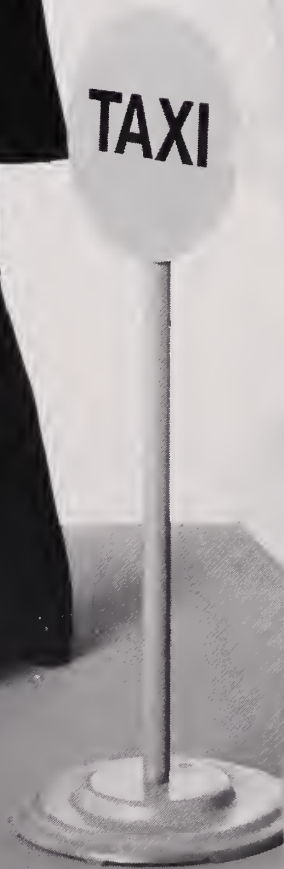


**antifungal**

**antipruritic**

**antibacterial**

**anti-  
inflammatory**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform® Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Use in Pregnancy

Though topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain. If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression. May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

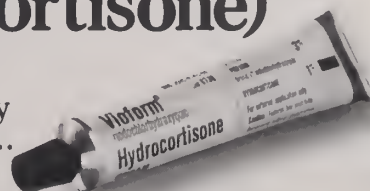
Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/6867 17

# Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

# Where do you stand on these issues?

Pro    Con

- |                          |                          |  |
|--------------------------|--------------------------|--|
| <input type="checkbox"/> | <input type="checkbox"/> | Maternal and child care programs                           |
| <input type="checkbox"/> | <input type="checkbox"/> | Federal aid to medical students                            |
| <input type="checkbox"/> | <input type="checkbox"/> | Extending private health insurance to everyone             |
| <input type="checkbox"/> | <input type="checkbox"/> | Nationwide program of community emergency medical services |
| <input type="checkbox"/> | <input type="checkbox"/> | Reform of the tort system of malpractice adjudication      |
| <input type="checkbox"/> | <input type="checkbox"/> | Maximum Allowable Cost (Drug) Regulations                  |
| <input type="checkbox"/> | <input type="checkbox"/> | Health Planning Act of 1974                                |
| <input type="checkbox"/> | <input type="checkbox"/> | Federal control of the number and location of residences   |
| <input type="checkbox"/> | <input type="checkbox"/> | Federal standards for licensure and re-licensure           |
| <input type="checkbox"/> | <input type="checkbox"/> | Federal national health service                            |

If you're for the first five but against the second five, you stand where the AMA stands.

The AMA has vigorously supported virtually all recent legislation to provide more and better health care for the public. The AMA has just as staunchly opposed any plan that would infringe on your right to practice the way you choose.

On such vital issues, the AMA is the most effective and influential spokesman the profession has. With your support, it can be even more effective.



**Join us.**

**We can do much more together.**

Dept. of Membership Development  
American Medical Association  
535 N. Dearborn St./Chicago, IL 60610

Please send me more information on the AMA and AMA membership.

Name \_\_\_\_\_

Address \_\_\_\_\_

City/State/Zip \_\_\_\_\_

# HYPERLIPOPROTEINEMIC TYPES AMONG PUERTO RICANS: A FINAL REPORT

Marta Cancio, Ph.D. and José M. León, BS, MT.

**Abstract:** This report summarizes the results of the study on hyperlipoproteinemic Puerto Rican subjects performed during an eight years period. Classification in types was done according to the World Health Organization. Distribution of cases by type was: 5 Type I, 258 Type IIa, 198 Type IIb, 186 Type IV and 76 Type V. Type I were all children of Caucasian race; 4 female, 1 male. Type IIa were mostly in their fifties, while Types IIb, IV and V peaked in number in their forties. Over 90 percent of cases in all types except Type V were Caucasian; in Types IIa, IIb, IV and V close to 90 percent or over of cases were male. In Type IV 78 percent were obese and 67 percent were diabetic. These conditions were also high (over 60 percent) in Type V. CVD was high (over 60 percent) in Types IIa and IIb. Over 60 percent of the cases of all types were from the Northern region of Puerto Rico.

**Resumen:** Se presenta un resumen de los resultados finales de un estudio de tipos hiperlipémicos entre puertorriqueños llevado a cabo durante un período de ocho años. Se clasificaron los casos siguiendo las recomen-

daciones de la Organización Mundial de la Salud. Un total de 723 casos fueron clasificados de acuerdo al tipo de hiperlipoproteinemia. La distribución de los casos de acuerdo al tipo es la siguiente: 5 Tipo I, 258 Tipo IIa, 198 Tipo IIb, 186 Tipo IV y 76 Tipo V. Se incluyen la distribución de los casos para cada grupo por edad, sexo, raza y datos sobre la incidencia de obesidad, diabetes, gota, enfermedades cardiovasculares y del riñón, hipertensión y otras condiciones. También se presenta la distribución geográfica de los casos.

In 1970 the World Health Organization published a memorandum on the classification of hyperlipidemias and hyperlipoproteinemias (1). Six abnormal lipoprotein patterns were described in a refinement of the original classification system of Fredrickson (2). Table I summarizes the most distinguishing features of each abnormal pattern.

Type I is defined as an abnormal accumulation of chylomicrons. Plasma obtained from individuals in the fasting state, when allowed to stand, show a cream layer over a clear infranatant. The paper electrophoretic pattern of such plasma shows a heavy chylomicron band.

Type IIa is characterized by an abnormal concentration of low-density lipoproteins. Standing plasma is clear. Paper electrophoresis shows an intensely staining beta-lipoprotein band.

Type IIb is distinguished by abnormal concentrations of both low-density and very low-density lipoproteins. The standing plasma

---

*From the Medical Research Laboratories, Veterans Hospital and Department of Biochemistry and Nutrition, University of Puerto Rico School of Medicine, San Juan, Puerto Rico 00936.*

*Supported in part by the Puerto Rico Heart Association (Grant in Aid).*

*Presented in part at the IX International Nutrition Congress, Mexico City, Mexico, September 1972.*

*Request reprints from: Dr. M. Cancio, Veterans Hospital, G. P. O. Box 4867, San Juan, Puerto Rico 00936.*



TABLE I  
SUMMARY OF LIPOPROTEIN ABNORMALITIES

Type	Appearance of Standing Plasma	PAPER ELECTROPHORETIC PATTERN			
		Chylomicrons	$\beta$ -lipoproteins	pre- $\beta$ lipoproteins	Floating $\beta$ -lipoproteins
I	cream layer over clear infranatant	+			
IIa	clear		+		
IIb	clear or faintly turbid		+	+	
III	turbid				+
IV	clear or turbid			+	
V	cream layer over turbid infranant	+		+	

is either clear or faintly turbid throughout, without a chylomicron cream layer on top. The paper electrophoretic pattern is characterized by intensely staining beta plus pre-beta lipoprotein bands.

Type III is defined as a separate pattern characterized by the presence of an abnormal class of lipoproteins: floating beta lipoproteins. Standing plasma is usually turbid, frequently with a faint chylomicron cream layer. The paper electrophoretic pattern shows a broad-beta band extending from the beta position into the pre-beta position. Confirmation of the presence of floating-beta lipoproteins should be made after preparative ultracentrifugation of the very low density lipoprotein fraction.

Type IV is characterized by abnormal concentrations of very low-density lipoproteins. Standing plasma is clear or turbid throughout with no chylomicrons on top. The paper electrophoretic pattern is distinguished by an intensely staining pre-beta lipoprotein band.

Type V is distinguished by the presence of chylomicrons and increased concentrations of very low-density lipoproteins. Standing plasma contains a chylomicron cream layer on top of a turbid infranatant layer. The paper electrophoretic pattern shows chylomicrons plus an increased pre-beta lipoprotein band.

The prevalence of various types of hyperlipidemia reported from different countries varies although the sampling techniques have differed which makes comparisons difficult. In Milan, Italy (3) out of a series of 478 hospitalized patients and outpatients the following percentages were found: Normal: 33.9, Type I: 0.8, Type II: 19.7, Type III: 0.8, Type IV: 40.6, Type V: 4.2. This distribution is identical to that reported by R. M. Iammarino of the Department of Pathology, University of Pittsburgh to the XIX Colloquium on Protides of the Biological Fluids, held at Bruges (4).

In Puerto Rico Gulbrandsen et al (5) studied serum lipoprotein patterns in a previously selected population of urban and rural Puerto

Rican men aged 45 to 64. Out of 1494 men aged 45 and over they found 708 (47 percent) normal; and out of 1385 men aged 45-64 the following percentages were reported: Type I: 0.0, Type II: 3.3, Type III: 0.1, Type IV: 18.6, Type V: 0.3, and mixed Type II and IV: 4.3.

A study of hyperlipoproteinemic types among Puerto Ricans utilizing the internationally accepted classification described by the W. H. O. has been performed. The following is a summary of the results obtained.

## MATERIALS AND METHODS

Study subjects were patients who, according to their physicians, were hyperlipemic suspects. Most of the patients were referred from the Veterans Administration Hospital. Outpatients from the University of Puerto Rico School of Medicine Hospital, as well as from private physicians were included.

Materials and methods used for the lipid profile have been described in detail in previous publications (6, 7, 8). Lipoprotein patterns were determined by means of paper electrophoresis in albumin containing buffer and stained with Oil Red O (9). Results were correlated with serum triglycerides (10), serum cholesterol (11), and appearance of standing plasma, in order to classify cases according to the guidelines of the W. H. O., as described above. Preparative ultracentrifugation of plasma, without changing its density, for 16 hours at 100,000 g (12, 13, 14) was performed in the case of Type III suspects by means of a Beckman Model L, preparative ultracentrifuge, with an SW 39 rotor. Tubes were sliced and the  $d < 1.006$  supernatant collected and processed for lipoproteins by paper electrophoresis, for cholesterol and triglycerides. Whole plasma was similarly analyzed.

Patients included in this report had at least two lipid profiles performed. Most patients had several profiles performed to assure accuracy of classification, specially if there was any doubt after the first two successive determinations.

All patients referred for hyperlipoproteinemic studies had a standardized study form filled. Part of the information in the form was filled by the patient's physician. Another part of the form was filled when patients were interviewed at the time of blood with-

drawal. The information included in the form was: patient's name, social security number, address, place of birth, age, race, family history, history of illnesses, weight, height, and blood pressure. Place of birth was obtained by town if born in Puerto Rico. This data was later classified according to regions as used by the Puerto Rico Department of Health (personal communication). The North region includes all towns in the North and East of the Island, comprising the Sub-Regions of Arecibo, Bayamón, Caguas, Metropolitan Area and Fajardo. The South Region includes all Southern towns in the vicinity of Ponce and Guayama. The West Region includes all Western towns comprising the Sub-Regions of Aguadilla and Mayagüez. Patients born outside Puerto Rico were classified by Country. Patient's race was classified as colored if the physical features, color or hair showed characteristics of the Negro or Indian races; all others were classified as Caucasian. (We realize the difficulty of having an adequate appraisal of race in Puerto Rico). Patients were weighed and measured for height. Obesity (20 percent or more over desirable weight) was determined utilizing the Weight and Height Tables from the Metropolitan Life Insurance Company, Statistical Bureau.

All other pertinent clinical information included in this report was obtained from the patient's clinical record. Patients with unconfirmed diagnosis of diabetes or gout were further evaluated by means of a glucose tolerance test and/or uric acid determinations.

All patients study forms were revised for completeness of information. Patients with incomplete data were excluded from this report.

Data was coded and punched utilizing a 318 SRP Punch Card System.

This study began in 1966 and was completed in 1974.

## RESULTS

Results were tabulated and shown in Tables 2 through 9. A total of 723 cases were classified. Distribution of cases according to hyperlipoproteinemic type is given in Table 2. The number of cases as well as the percent of total number of cases is given for each type. No Type III cases were confirmed after preparative ultracentrifuga-

TABLE II  
DISTRIBUTION OF HYPERLIPEMIC CASES BY TYPE

Type	No.. of Cases	Percent of Total
<i>I</i>	5	0.7
<i>IIa</i>	258	35.7
<i>IIb</i>	198	27.4
<i>III</i>	0	0.0
<i>IV</i>	186	25.7
<i>V</i>	76	10.5
<i>Total</i>	723	100.0

TABLE III  
DISTRIBUTION OF HYPERLIPEMIC CASES BY AGE

Type	Age Group (years)	No. of Cases	Percent
<i>I</i>	< 30	5	100
<i>IIa</i>	< 30	9	4
	30-39	29	11
	40-49	81	31
	50-59	115	45
	> 60	24	9
<i>IIb</i>	< 30	2	1
	30-39	25	13
	40-49	85	43
	50-59	67	34
	> 60	19	9
<i>IV</i>	< 30	6	3
	30-39	28	15
	40-49	77	41
	50-59	63	34
	> 60	12	7
<i>V</i>	< 30	6	8
	30-39	23	30
	40-49	32	42
	50-59	15	20

tion of the very - low - density lipoprotein fraction.

Distribution of cases in each type according to age is given in Table 3. Likewise, distribution

by race and sex is presented in Table 4.

Incidence of various clinical conditions, in addition to the lipidic disorders reported here, is given in Tables 5 through 8. The following



**TABLE IV**  
**DISTRIBUTION OF HYPERLIPEMIC CASES BY RACE AND SEX**

<i>Type</i>	<i>Race</i>	<i>Sex</i>	<i>No. of Cases</i>	<i>Percent</i>
<i>I</i>	<i>Caucasian</i>		5	100
		<i>male</i>	1	20
		<i>female</i>	4	80
<i>IIa</i>	<i>Caucasian</i>		234	91
	<i>Colored</i>		24	9
		<i>male</i>	233	90
		<i>female</i>	25	10
<i>IIb</i>	<i>Caucasian</i>		183	92
	<i>Colored</i>		15	8
		<i>male</i>	188	95
		<i>female</i>	10	5
<i>IV</i>	<i>Caucasian</i>		176	95
	<i>Colored</i>		10	5
		<i>male</i>	180	97
		<i>female</i>	6	3
<i>V</i>	<i>Caucasian</i>		65	86
	<i>Colored</i>		11	14
		<i>male</i>	68	89.5
		<i>female</i>	8	10.5

**TABLE V**  
**INCIDENCE OF OBESITY, DIABETES AND GOUT**  
**AMONG HYPERLIPEMIC CASES**

<i>Type</i>	<i>Clinical Condition</i>	<i>Present in</i>	<i>Percent</i>
<i>IIa</i>	<i>Obesity</i>	157	59
	<i>Diabetes</i>	98	38
	<i>Gout</i>	17	7
<i>IIb</i>	<i>Obesity</i>	119	60
	<i>Diabetes</i>	111	56
	<i>Gout</i>	39	20
<i>IV</i>	<i>Obesity</i>	145	78
	<i>Diabetes</i>	124	67
	<i>Gout</i>	43	23
<i>V</i>	<i>Obesity</i>	52	68
	<i>Diabetes</i>	46	61
	<i>Gout</i>	13	17

TABLE VI  
INCIDENCE OF HYPERTENSION, CARDIOVASCULAR DISEASE  
AND KIDNEY DISEASE AMONG HYPERLIPEMIC CASES

Type	Clinical Condition	Present in	Percent
IIa	Hypertensive	86	33
	CVD	165	64
	Kidney disease	2	1
IIb	Hypertensive	88	44
	CVD	128	65
	Kidney disease	13	7
IV	Hypertensive	86	46
	CVD	108	58
	Kidney disease	12	6
V	Hypertensive	44	58
	CVD	35	46
	Kidney disease	8	10

clinical conditions are included: obesity, diabetes and gout (Table 5); hypertension, cardiovascular and renal disease (Table 6); abdominal pain, pancreatitis, alcoholism and liver disease (Table 7).

Geographic distribution for each of the hyperlipemic types, by region is given in Table 9.

## DISCUSSION

The current usefulness of lipoprotein phenotyping by electrophoresis has been re-examined by Fredrickson in a recent editorial (15). The discovery and treatment of hyperlipidemia is now an established part of the practice of preventive cardiology. Definitive proof is still lacking that the resulting change in life style for many people will be rewarded by a decrease in the risk of premature ischemic heart disease. The circumstantial evidence for a probable benefit to many is overwhelming, and the risk factor deserves the attention it is now receiving. The general validity of the usefulness of lipoprotein phenotyping has not changed.

The majority of hyperlipemic cases among the cases studied by us were classified as Types

IIa, IIb and IV, followed by Type V. The small number of Type I cases is not surprising since the Type I pattern is considered rare (15). No cases with the unusual Type III anomaly were confirmed after preparative ultracentrifugation of the very - low - density lipoprotein fraction (Table 2).

Expression of Type I usually occurs in childhood (12). All of our Type I cases were children. In their study of serum lipoprotein patterns in Puerto Rican men Gulbrandsen et al (5) found that the prevalence of Type II was greater in the older (55-64) than the younger (45-54) urban group while the prevalence of Type IV was slightly greater in the younger than in the older urban group. In the present study distribution of cases by decades showed a higher prevalence of Type IIa in the 50-59 age group, while Types IIb and IV were more prevalent in the 40-49 group. Type V usually occurs in young adults (12). Our Type V cases were more prevalent in the 40-49 group (Table 3).

There seems to be no difference in the prevalence of hyperlipemia due to sex or race. In a compilation from the literature on Type I

TABLE VII  
INCIDENCE OF ABDOMINAL PAIN, PANCREATITIS, ALCOHOLISM  
AND LIVER DISEASE AMONG HYPERLIPEMIC CASES

Type	Clinical Condition	Present in	Percent
I	Abdominal pain	4	80
	Pancreatitis	0	0
	Alcoholism	0	0
	Liver disease	0	0
IIa	Abdominal pain	62	24
	Pancreatitis	2	1
	Alcoholism	2	1
	Liver disease	12	5
IIb	Abdominal pain	49	25
	Pancreatitis	0	0
	Alcoholism	2	1
	Liver disease	11	6
IV	Abdominal pain	60	32
	Pancreatitis	3	2
	Alcoholism	5	3
	Liver disease	12	6
V	Abdominal pain	19	25
	Pancreatitis	4	5
	Alcoholism	4	5
	Liver disease	6	8

hyperlipoproteinemia Fredrickson found 17 female and 15 male patients. No data is given regarding race (12). In this study the five Type I cases reported were white of which four were female. The only male case is the brother of one of the female cases. Over 90 percent of our Type II and IV cases were white\*males. Fredrickson et al (12) presented data on 22 patients with familial Type V hyperlipoproteinemia. Among parents and adult sibs there were 15 male and 8 female Type V cases, and 18 male and 14 female Type IV cases. No obvious concentration among any particular ethnic

group was noted, although all the families studied were white. In our Type V group over 80 percent of cases were white males (Table 4).

Gulbrandsen reported that Puerto Rican men with Types II and IV were obese (5). In the present study we found that the majority of hyperlipemic patients in Types II, IV and V were obese. Among the Type V cases the incidence of obesity was 78 percent, higher than in all other groups. Type I patients are usually not obese (12).. None of our Type I cases was overweight (Table 5).

Abnormal glucose tolerance has been reported in 50 percent of Type IV cases and in approximately 90 percent of Type V cases (16). In the present report it was found that the inci-

(The 1950 census classified the population of Puerto Rico as 79.7 percent white and 20.2 percent Negro; Encyclopedia Britannica 18: 853, 1972).



TABLE VIII  
INCIDENCE OF OTHER CLINICAL CONDITIONS AMONG  
HYPERLIPEMIC CASES

Type	Clinical Condition	Present in	Percent
IIa	Xanthomas	1	0.4
	Neuropsychiatric disease	6	2.3
	Thyroid disease	5	1.9
IIb	Xanthomas	1	0.5
	Neuropsychiatric disease	10	5.0
	Thyroid disease	2	1.0
IV	Xanthomas	2	1.1
	Neuropsychiatric disease	7	3.8
	Thyroid disease	3	1.6
V	Xanthomas	6	7.9
	Neuropsychiatric disease	5	6.6
	Thyroid disease	1	1.3

dence of diabetes was higher among the Type IV patients (67 percent). In Types V (61 percent) and IIb (56 percent) the incidence of diabetes was also high. It was lower among the Type IIa cases (38 percent) (Table 5).

Gout and its relation to lipid metabolism was studied by Mielants et al in 31 patients with primary gout (17). A statistically significant increase of the pre-beta lipoproteins was found in the gouty patients. These findings suggest an association between hyperuricemia and hyperlipidemia. The importance of lipid and lipoprotein determinations in cases of primary gout is emphasized by these investigators. Hyperuricemia has been reported in 41 percent of subjects with familial Type V (12). In this study hyperuricemia was relatively high in Types IV (23 percent), IIb (20 percent) and V (17 percent), being lower in Type IIa (7 percent) (Table 5).

Hyperlipidemia in coronary heart disease was studied in 500 survivors of myocardial infarction by Goldstein et al (18), 31 percent

of which had hyperlipidemia. These lipid abnormalities were most commonly found in males under 40 years of age (60 percent frequency) and in females under 50 years of age (60 percent frequency). Elevation in triglyceride levels with (7.8 percent) or without (15.6 percent) an associated elevation in cholesterol levels was three times more common in survivors than a high cholesterol level alone (7.6 percent). Our data shows that the group with a higher incidence of hypertension was Type V (58 percent). The incidence of cardiovascular disease was high in Types IIb (65 percent) and IIa (64 percent), moderately high in Type IV (58 percent), and lower in Type V (46 percent) (Table 6).

The nephrotic syndrome has been associated with Types II, IV and V (1). In this study kidney disease was present in 10 percent of Type V, 7 percent of Type IIb, 6 percent of Type IV and 1 percent of Type IIa cases (Table 6).

Episodic abdominal pain may occur in all

TABLE IX  
ORIGIN OF THE HYPERLIPEMIC SUBJECTS

Place of Birth (Region) *	HYPERLIPEMIC TYPE									
	I		IIa		IIb		IV		V	
	No.	(Percent)	No	(Percent)	No	(Percent)	No.	(Percent)	No.	(Percent)
Puerto Rico -										
North	4	(80)	167	(65)	116	(58)	120	(65)	54	(71)
South			33	(13)	36	(18)	30	(16)	7	(9)
West			36	(14)	21	(11)	26	(14)	11	(15)
Outside P. R. **	1	(20)	22	(8)	25	(13)	10	(5)	4	(5)
** Place of Birth (Country)										
U. S. A.	(1)	***	10	(2)***	17	(2)***	9	(5)***	3	(1)***
V. I.			6		1					
Cuba			3		3					
Dom. Rep.			2		2		1		1	
Italy					1					
Mexico					1					
Spain			1							

\*\*\* (No, P. R. parents)

\* As used by the P. R. Department of Health for Nutritional Studies.

types of hyperglyceridemia and is very common in Type I (12). In this study, abdominal pain was prevalent in four out of the five Type I cases. The other case was asymptomatic; he is the brother of one of the other cases (7, 8). Among the other hyperlipemic groups the incidence of abdominal pain was 32 percent in Type IV, 25 percent in Types IIb and V, respectively, and 24 percent in Type IIa (Table 7).

Pancreatitis and hyperlipemia has been studied among others by Kessler et al (19), Cameron et al (20) and Farmer, et al (21). The latter investigators conclude that the most consistent feature of one kind of pancreatitis is hyperlipoproteinemia with chylo-

micronemia. This condition probably occurs more frequently than has been previously recognized. Because of the favorable response to a low fat diet, this kind of pancreatitis can be treated adequately and further recurrence prevented. Pancreatitis was recorded by us in 5 percent of Type V, 2 percent of Type IV and 1 percent of Type IIa cases (Table 7).

Alcoholism has been generally associated with secondary hyperlipoproteinemia (16). The frequency of alcoholism among the cases studied by us was 5 percent in Type V, 3 percent in Type IV and 1 percent in Types IIa and IIb, respectively. Personal interview of patients reflected that most patients were "so-

cial drinkers", \* specially those in Type V (Table 7).

Hepatosplenomegaly may be present in Type IV and is more common in Type V (12). In this study liver disease was present in 8 percent of Type V, 6 percent of Types IV and IIb, respectively, and 5 percent of Type IIa cases (Table 7).

Xanthomas have been reported in Type II (as many as 80 percent of patients with essential familial Type II may have xanthomas before death), and in 15 percent of Type IV and 45 percent of Type V (12). The incidence of xanthomas in this study was 7.9 percent in Type V, 1.1 percent in Type IV, 0.5 percent in Type IIb and 0.4 percent in Type IIa (Table 8).

Neuropsychiatric conditions have not been associated in the literature with hyperlipoproteinemias. In the cases included in this report neuropsychiatric conditions were present in 6.6 percent of Type V, 5 percent of Type IIb, 3.8 percent of Type IV and 2.3 percent of Type IIa patients (Table 8). \*\*

Hypothyroidism has been associated with Types II and IV (1). In this study thyroid disease was present in 1.9 percent of Type V, and 1.0 percent of Type IIb cases (Table 8).

In conclusion we have reported 723 cases with hyperlipoproteinemia in Puerto Rico. The frequency of obesity was higher among the Type IV patients, although it was high also in Types IIa, IIb and V. Diabetes was also higher among the Type IV cases, being high also in Types IIb and V. Cardiovascular diseases were higher in Types IIa and IIb, followed in frequency by Type IV. The association of

hyperlipidemia with obesity, diabetes and cardiovascular diseases in these patients points out once more the importance of the measurement and control of serum lipids and lipoproteins in clinical practice.

## ACKNOWLEDGMENT

We thank Miss Judith Reyes and Mrs. Sonia Esterrich for technical assistance, the physicians who referred cases for study, the dietitians of the Veterans Hospital, specially Mrs. Paquita Haddock de Agosto (Diet Therapy, Education and Research Section Chief, Dietetic Service) for their constant interest and encouragement, and Mrs. María V. Lara (Chief, Nutrition Program, Puerto Rico Health Department) for providing us the information regarding the regions of Puerto Rico as used by the Department of Health for Nutritional Studies. We also thank patients, without whose cooperation this study would have been impossible. Thanks are due also to Dr. Efraín Toro-Goyco (Professor and Chairman, Department of Biochemistry and Nutrition of the School of Medicine) and Dr. Nelson Fernández (Assistant Professor, Department of Biochemistry and Nutrition of the School of Medicine) for reviewing the manuscript and for valuable suggestions.

## REFERENCES

1. Beaumont, J. L., Carlson, L. A., Cooper, G. R., Fejfar, Z., Fredrickson, D. S. and Strasser, T.: Classification of hyperlipidaemias and hyperlipoproteinaemias. *Bull Wld Hlth Org* 43: 891, 1970.
2. Fredrickson, D. S.: A system for phenotyping hyperlipoproteinemia. *Circulation* 31: 321, 1965.
3. Vergani, C., Vecchi, G., Pugno Vanoni, R.: Serum lipoprotein distribution in normal children and adults of different ages. *Prot Biol Fluids*, XIX Colloquium, Brugge, 1971.
4. Dioguardi, N. and Vergani, C.: Introduction on human hyperlipoproteinemias. Human hyperlipoproteinemias. Principles and Methods. Edited by R. Fumagalli, G. Ricci, and S. Gorini. *Advances in Experimental Medicine and Biology* 38: 10, Plenum Press, New York, 1973.
5. Gulbrandsen, C. L., García Palmieri, M. R., Tillotson, J., Nazario, E., Costas, R. and Colón, A. A.: Serum lipoprotein patterns in Puerto Rican men. *Bol Asoc Med P Rico* 67: 148, 1975.
6. Cancio, M.: The serum lipid picture. *Bol Asoc Med P Rico* 58: 563, 1966.
7. Maldonado, N., Frías, A. E., Cancio, M., Gulbrandsen, C. and Haddock, J.: Type I Hyperlipoproteinemia. *Bol Asoc*

\* A social drinker is one who drinks one, two, or three but less than four ounces of 80 proof liquor at one sitting on occasion-and-without getting drunk. (Kaye, Sidney. *Military Medicine* 141: 604, 1976).

\*\* In 1976 there were approximately 14 percent of neuropsychiatric disorders in the general admissions to the VA Hospital.



Med P Rico 62: 301, 1970.

8. Cancio, M. and León, J. M.: Hyperlipoproteinemic types among Puerto Ricans: A progress report. Bol Asoc Med P Rico 64: 11, 1972.
9. Lees, R. S. and Hatch, F. T.: Sharper separation of lipoprotein species by paper electrophoresis in albumin-containing buffer. J Lab Clin Med 61: 518, 1963.
10. Van Handle, E. and Zilversmit, D. B.: Micromethod for direct determination of serum triglycerides. J Clin Med 50: 152, 1957.
11. Zak, B.: Simple rapid microtechnic for serum total cholesterol. Arner J Clin Path 27: 583, 1957.
12. Fredrickson, D. S. and Levy, R. I.: Basis of Inherited Disease. Edited by John B. Stanbury, James B. Wyngaarden and Donald S. Fredrickson. Third Edition: pp 545-614 McGraw-Hill Book Co., New York, 1972.
13. Levy, R. I. and Fredrickson, D. S.: Diagnosis and management of hyperlipoproteinemia. Am J Cardiol 22: 576, 1968.
14. Hazzard, W. R., Porte, Daniel and Bierman, E. L.: Abnormal lipid composition of very low density lipoproteins in diagnosis of broad-beta disease (Type III Hyperlipoproteinemia). Metabolism 21: 1009, 1972.
15. Fredrickson, D. S.: It's time to be practical. Circulation 51: 205, 1975.
16. Levy, R. I. and Glueck, C. J.: Hypertriglyceridemia, diabetes mellitus, and coronary vessel disease. Arch Intern Med 123: 220, 1969.
17. Mielants, H., Veys, E. M. and De Weerd, A.: Gout and its relation to lipid metabolism. I. Serum uric acid, lipid and lipoprotein levels in gout. Ann Rheum Dis 32: 501, 1973.
18. Goldstein, J. L., Hazzard, W. R., Schrott, H. C., Bierman, E. L. and Motulsky, A. G.: Hyperlipidemia in coronary heart disease. I. Lipid levels in 500 survivors of myocardial infarction. J Clin Invest 52: 1533, 1973.
19. Kessler, J. L., Miller, M., Barza, D. and Mishkin, S.: Hyperlipemia in acute pancreatitis. Am J Med 42: 968, 1967.
20. Cameron, J. L., Crisler, C., Margolis, S., De Meestes, T. R. and Zuidema, G. D.: Acute pancreatitis with hyperlipemia. Surgery 70: 53, 1971.
21. Farmer, R. C., Winkelman, E. I., Brown, H. B. and Lewis, L. A.: Hyperlipoproteinemia and pancreatitis. Am J Med 54: 161, 1973.

# FACTORES SOCIOEPIDEMIOLOGICOS DEL USO DE DROGAS ENTRE LOS ESTUDIANTES DE LAS ESCUELAS SECUNDARIAS DE PUERTO RICO

Rafaela Robles, Ed.D., Ruth Martínez, B.A., Ana I. Colón, B.A. y Margarita Moscoso, B.A.

**Abstract:** The findings of the first wave of a longitudinal study on socioepidemiological factors related to the use of drugs among secondary school students in Puerto Rico are presented. The data specifies the prevalence of the use of licit and illicit drugs among the students and the relation of this behavior with variables such as sex, interpersonal relation with peers, grade average, religious attendance, migratory experience and self-perception of health and happiness. The results of the study are also compared with evidence available from scientific investigations on the use of drugs among adolescent students in the United States.

**Resumen:** Se presentan los hallazgos de la primera fase de un estudio longitudinal sobre los factores socioepidemiológicos del uso de drogas entre la población estudiantil de las escuelas secundarias de Puerto Rico. Se especifica la prevalencia de uso de drogas lícitas e ilícitas entre los estudiantes y la relación de esta conducta con variables tales como sexo, relación con pares, índice académico, asistencia a servicios religiosos, experiencia migratoria y percepción de salud y felicidad propia. También se discuten los datos en comparación con evidencia obtenida en investigaciones sobre el uso de drogas entre estudiantes adolescentes en Estados

Unidos.

La comunidad científica ha especificado diferentes trastornos físicos y mentales que están relacionados con el uso y abuso de diferentes drogas lícitas e ilícitas. Estos hallazgos han ayudado a contestar muchas preguntas sobre la etiología, control y prevención de varios grupos de enfermedades de alta prevalencia en diferentes países del mundo incluyendo a Puerto Rico.

Sin embargo, la utilización efectiva de estos hallazgos dependerá de la aportación que hagan los estudios epidemiológicos para determinar la relación entre el uso de drogas y las variables socioculturales relevantes a esta conducta. Es necesario especificar la prevalencia de uso de drogas en la población, las características de los grupos con mayor prevalencia, las estructuras de las redes familiares, de los amigos o conocidos en los diferentes grupos estudiados y sus normas, valores y percepciones.

Estos hallazgos socioepidemiológicos ofrecerán las bases para el desarrollo y evaluación de programas de servicio, ya sean clínicos o educativos, a niveles individuales, familiares y comunales.

En Puerto Rico, se han desarrollado múltiples programas de servicio y educación relacionados con el uso de drogas por la juventud. Sin embargo, hasta el presente la Isla carece de estudios socioepidemiológicos que puedan servir de base para orientar la política pública y planificar, desarrollar y evaluar programas educativos y de servicio para este grupo pobla-

---

*De la Escuela Graduada de Salud Pública, Recinto de Ciencias Médicas, Universidad de Puerto Rico, San Juan, Puerto Rico.*

*Este estudio fue auspiciado por el "National Institute of Drug Abuse", Concesión Número RO1 DA 00635-03.*

cional.

Este informe presenta los hallazgos de la primera fase de un estudio longitudinal llevado a cabo durante los años 1974 y 1975, entre la población estudiantil de las escuelas secundarias de Puerto Rico.

El estudio tiene como finalidad determinar los factores asociados con el uso de drogas por los estudiantes y la relación de esta conducta con la transición de escuela intermedia a escuela superior. Se definió el término droga como una sustancia de efecto estimulante, deprimente o narcótico, que puede causar dependencia física o psicológica. Se investigó sobre el uso de las siguientes drogas: inhalantes, marihuana, agentes psicodélicos, anfetaminas, heroína, alcohol y cigarrillos.

Esta información podrá ser útil para formular la política pública respecto al uso de drogas por la juventud. Los hallazgos también podrían utilizarse en la planificación y evaluación de programas de servicios para la población estudiantil.

## METODO

El estudio se llevó a cabo en las escuelas públicas y privadas en once pueblos de la Isla. Los pueblos participantes se escogieron y agruparon en cuatro categorías en base al tamaño de la población.

Se seleccionó una muestra probabilística estratificada por localización, tamaño y niveles de las escuelas. El tamaño final de la muestra, 18,712 entrevistados, consiste de 16,103 estudiantes de los grados nueve al doce en las escuelas públicas y 2,609 estudiantes de los grupos ocho al doce en las escuelas privadas. Cada participante fue entrevistado dos veces: una vez por año durante los dos años consecutivos del estudio. La información se obtuvo a través de un cuestionario que se administró simultáneamente a todos los grupos de las escuelas durante un período de clase.

Estudiantes universitarios adiestrados en técnicas de entrevistas sustituyeron a los maestros durante el período de recolección de datos. Los cuestionarios fueron anónimos. Se usó una clave para parear las contestaciones de los entrevistados en las dos fases del estudio. Este método ha sido usado por otros investigadores en Estados Unidos con el propósito de proteger la confidencialidad de la información ofrecida por los estudiantes. Esta técnica de identificación fue

sometida a prueba en una escuela de Puerto Rico antes de ser adoptada para el estudio.

## RESULTADOS

El 52.3 por ciento de los estudiantes de las escuelas secundarias de Puerto Rico informan haber usado drogas. Como indica el Cuadro I, el alcohol y los cigarrillos son las drogas más usadas por los estudiantes. El 44 por ciento de los estudiantes informó uso de alcohol y 27.9 por ciento uso de cigarrillos.

Al sumar los porcentajes de los usuarios de las diferentes drogas ilícitas, ya sean solas o en combinación con otras drogas, se encuentra que alrededor de uno de cada ocho estudiantes ha usado drogas ilícitas alguna vez (11.8 por ciento). La marihuana es la droga ilícita con mayor frecuencia de uso (7.0 por ciento).

### *Escuelas Públicas y Privadas*

Al comparar ambos sistemas escolares se encontró que la frecuencia de uso de drogas, lícitas e ilícitas, es más alta en las escuelas privadas (Figura I y II). Dos de cada tres estudiantes de las escuelas privadas han usado drogas (68.4 por ciento). En las escuelas públicas la proporción es de uno de cada dos estudiantes (49.5 por ciento).

Uno de cada seis estudiantes en las escuelas privadas informan haber usado drogas ilícitas (16.6 por ciento). En las escuelas públicas la proporción de estudiantes que han usado drogas ilícitas es uno de cada diez (10.8 por ciento).

El análisis de los datos por sexo indica que la frecuencia de uso de drogas ilícitas es mayor tanto en los varones como en las hembras de las escuelas privadas (20.8 por ciento y 11.9 por ciento, respectivamente) que sus pares del mismo sexo en las escuelas públicas (15.6 por ciento varones y 7.0 por ciento hembras).

El uso de alcohol por los adolescentes de las escuelas privadas es mayor que el de



**CUADRO I**  
**USO DE DROGAS ENTRE LOS ESTUDIANTES DE LAS ESCUELAS SECUNDARIAS**  
**(TOTAL DE LA MUESTRA – PRIMERA FASE, 1974 \*)**

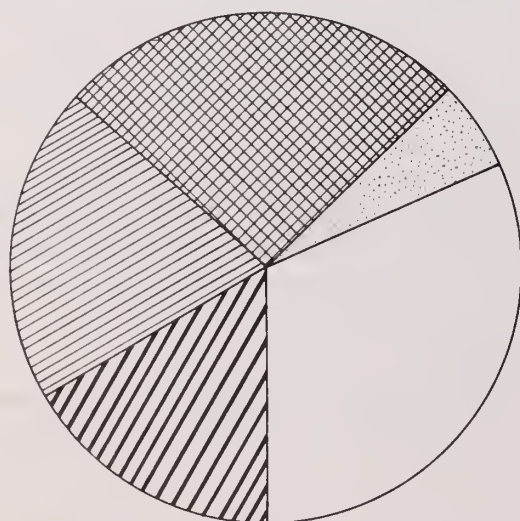
*n* = 18,562 \*\*

TIPO DE DROGA	Distribución de Frecuencia y Por Ciento de Uso de Drogas	
	N	Por Ciento
No usuarios	8863	47.7
Cigarrillos	5183	27.9
Alcohol	8176	44.0
Pega	751	4.0
Cocaína	316	1.7
Marihuana	1308	7.8
Psicodélicos	369	2.0
Depresivos	818	4.4
Estimulantes	418	2.3

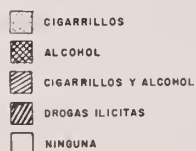
\* Uso de la droga sola o en combinación con otra.

\*\* Para todos los cuadros y figuras, el total de la muestra es 18,712 con variaciones debido a respuestas múltiples y data no informada.

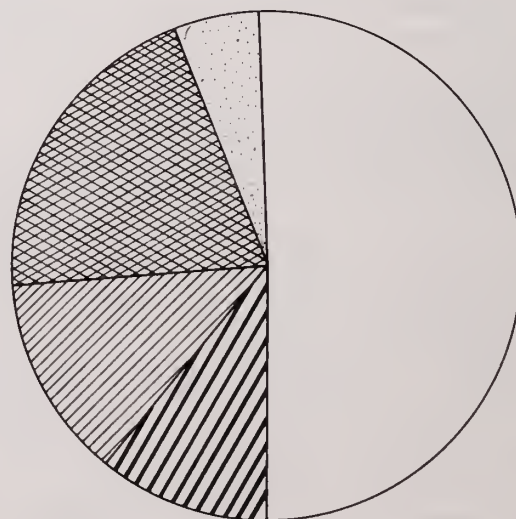
**FIGURA I**  
**USO DE DROGAS POR ESCOLARES ADOLESCENTES**  
**SISTEMA PRIVADO DE ENSEÑANZA**  
**N = 2,588**



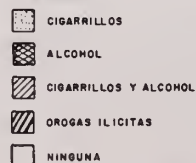
**LEYENDA**



**FIGURA II**  
**USO DE DROGAS POR ESCOLARES ADOLESCENTES**  
**SISTEMA PUBLICO DE ENSEÑANZA**  
**N = 15,939**



**LEYENDA**



sus pares de las escuelas públicas independientemente del sexo. La frecuencia de uso de alcohol entre los sexos se distribuye de la siguiente manera en las escuelas privadas, 26.6 por ciento los varones y 25.2 por ciento las hembras. Entre los adolescentes de las escuelas públicas la distribución es de 22.5 por ciento en los varones y 18.6 por ciento en las hembras.

En ambos sistemas escolares se encontró que aquellos adolescentes que usan drogas tienden a asociarse con adolescentes que también las usan. Esta relación se manifiesta para todas las drogas estudiadas. La relación entre los adolescentes que usan drogas ilícitas y los amigos que usan marihuana aparece de la siguiente manera.

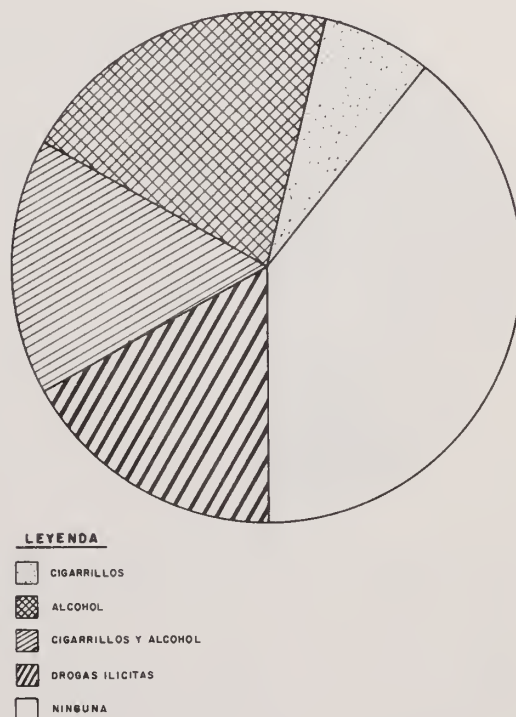
En las escuelas privadas el 31.4 por ciento de los estudiantes que usan drogas ilícitas informan que la mayor parte de sus amigos usan marihuana. El 46.8 por ciento informan que algunos de sus amigos usan esta droga.

En las escuelas públicas el 26.0 por ciento de los estudiantes que usan drogas ilícitas informan que la mayor parte de sus amigos usan marihuana y el 47.8 por ciento informan que algunos de sus amigos la usan.

El índice académico del estudiante y la asistencia a servicios religiosos resultaron estar relacionados con el uso de drogas entre los adolescentes. El uso de drogas ilícitas por los adolescentes de ambos sistemas escolares es mayor entre los estudiantes con índice académico bajo el promedio (18.9 por ciento en las escuelas públicas y 34.1 por ciento en las privadas) que entre aquellos con índice académico sobre el promedio (9.8 por ciento y 11.7 por ciento, respectivamente).

Los datos relativos a la variable asistencia a servicios religiosos revelan que entre los estudiantes de las escuelas privadas que usan drogas ilícitas, el número de adolescentes que nunca asiste a servicios religiosos es tres veces mayor que aquellos que dicen asistir frecuentemente (32.3 por ciento en comparación con 10.0 por ciento). Esta proporción es un poco más baja para los estudiantes de las escuelas públicas (20.2 por ciento y 7.7

FIGURA III  
USO DE DROGAS POR ESCOLARES ADOLESCENTES  
QUE HAN VIVIDO FUERA DE PUERTO RICO  
N = 5, 589



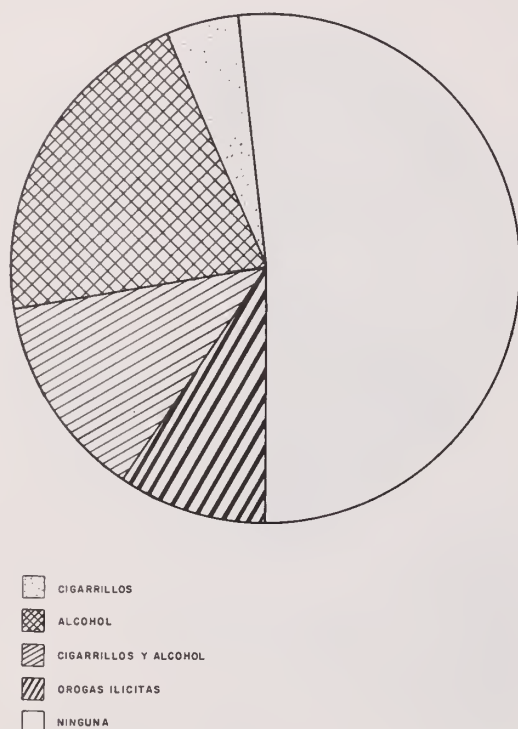
por ciento, respectivamente.

El uso de drogas ilícitas es mayor entre los adolescentes que han vivido fuera de Puerto Rico por un período de 6 meses o más (16.9 por ciento, Figura III) que entre aquellos que no han vivido fuera de la Isla (9.3 por ciento, Figura IV).

Entre las variables estudiadas se incluyeron varios aspectos de la salud física y mental de los adolescentes. En este informe se presentan los datos de la percepción que tiene el estudiante de su salud y felicidad y su relación con el uso de drogas (Cuadros II y III).

Una mayor frecuencia de los adolescentes de ambos sistemas escolares que usan drogas ilícitas se perciben con salud pobre e infelices. Contrario a estos resultados, el uso de alcohol está relacionado con diferentes percepciones en ambos sistemas escolares. Los estudiantes de las escuelas públicas que usan alcohol tien-

FIGURA IV  
USO DE DROGAS POR ESCOLARES ADOLESCENTES  
QUE NUNCA HAN VIVIDO FUERA DE PUERTO RICO  
N = 12,932



den a percibirse menos saludables y más infelices. En las escuelas privadas, los estudiantes que usan alcohol tienden a percibirse significativamente más saludables, y felices (Cuadros II y III).

## DISCUSION

El 52.3 por ciento de los estudiantes de las escuelas secundarias de Puerto Rico informaron haber usado drogas. El alcohol fue la droga más usada seguida por los cigarrillos y la marihuana. La frecuencia de uso de drogas ilícitas ascendió a 11.8 por ciento. La marihuana es la droga ilícita con mayor frecuencia de uso (7 por ciento).

Todo parece indicar que el estudiante adolescente puertorriqueño, aunque con una frecuencia de uso significativamente más baja, se asemeja a su par norteamericano en el orden de frecuencia de la clase de droga usada. En Estados Unidos al igual que en Puerto Rico la droga más usada por los estudiantes es el alcohol, seguida por los cigarrillos y la marihuana (Josephson, 1974) (1).

En un estudio longitudinal realizado por Johnston desde 1966 hasta 1970 con una muestra nacional de estudiantes varones de escuelas secundarias de Estados Unidos, encontró que el alcohol y los cigarrillos son las drogas más usadas por esa población (Johnston, 1973) (2). Un 21 por ciento de la muestra había usado marihuana alguna vez durante sus años en la escuela secundaria. Josephson informa que en 1971 y 1972 el 50 por ciento de los adolescentes norteamericanos estudiados habían tomado licor fuera del ámbito familiar. Una

CUADRO II  
USO DE DROGAS POR LOS ESTUDIANTES POR SISTEMA ESCOLAR  
Y PERCEPCION DE SU SALUD

DROGAS USADAS	Percepción de la Salud					
	SISTEMA PUBLICO			SISTEMA PRIVADO		
	Buena Por Ciento	Regular Por Ciento	Pobre Por Ciento	Buena Por Ciento	Regular Por Ciento	Pobre Por Ciento
No usuarios	50.9	50.2	35.7	32.2	27.8	30.0
Cigarrillos	5.4	5.6	6.3	5.6	7.4	0.0
Alcohol	33.1	33.7	35.0	46.6	43.3	20.0
Drogas Ilícitas	10.6	10.5	23.0	15.6	21.5	50.0
Total Por Ciento	100.0	100.0	100.0	100.0	100.0	100.0
Total N	11151	4460	283	2295	270	20



**CUADRO III**  
**USO DE DROGAS POR LOS ESTUDIANTES POR SISTEMA ESCOLAR Y**  
**PERCEPCION DE SU FELICIDAD**

<i>DROGAS USADAS</i>	<i>Percepción de la Felicidad</i>			
	<i>SISTEMA PUBLICO</i>		<i>SISTEMA PRIVADO</i>	
	<i>Feliz Por Ciento</i>	<i>No Feliz Por Ciento</i>	<i>Feliz Por Ciento</i>	<i>No Felix Por Ciento</i>
<i>No Usuarios</i>	52.0	34.0	32.3	26.0
<i>Cigarrillos</i>	5.2	8.0	5.6	7.0
<i>Alcohol</i>	33.0	37.4	46.5	41.0
<i>Drogas Ilícitas</i>	9.8	20.6	15.6	26.0
<i>Total Por Ciento</i>	100.0	100.0	100.0	100.0
<i>Total N</i>	14410	1353	2366	200

cuarta parte del grupo usaba cigarrillos en 1971 y una quinta parte en 1972. La marihuana, al igual que el alcohol, mantuvo el mismo por ciento de uso para ambos años (15 por ciento) (Josephson, 1974) (1).

Es interesante notar que el adolescente puertorriqueño no solamente se parece al estudiante norteamericano en el orden de las drogas que usa frecuentemente, sino también en el hecho de que la marihuana se ha unido al alcohol y al cigarrillo como una de las drogas más usadas. Aunque la frecuencia de uso de marihuana más reciente en Estados Unidos es el doble de la frecuencia en Puerto Rico (15 por ciento en Estados Unidos, 7 por ciento en Puerto Rico), la brecha entre ambos grupos de adolescentes en el uso de alcohol se está cerrando (50 por ciento en Estados Unidos, 44 por ciento en Puerto Rico).

Es importante señalar la semejanza en frecuencia de uso de alcohol entre los varones y hembras de las escuelas privadas en contraste con la disparidad en frecuencia de uso entre las hembras de ambos sistemas escolares. Es posible que la disparidad en la frecuencia de uso de alcohol entre las hembras de ambos sistemas escolares esté relacionada con el grado de diferenciación en los procesos socializadores y estilos de vida de los dos grupos socioeconómi-

cos a que pertenecen estas adolescentes. En el caso de las drogas ilícitas, la diferencia en frecuencia de uso entre los sexos es evidente en ambos sistemas escolares.

La posible relación entre el uso de drogas y los grupos primarios a que pertenece el individuo es una de las áreas más estudiadas en las investigaciones de esta conducta de los adolescentes. El hallazgo más consistente en esta área de investigación es que el adolescente que usa drogas tiende a tener amigos que también las usan.

En Puerto Rico este hallazgo fue comprobado en ambos sistemas escolares y consistentemente para todas las drogas. Investigaciones realizadas en Estados Unidos identifican el uso de drogas por los amigos como mejor pronosticador de uso de drogas entre los adolescentes que el uso por sus padres (Kandel, 1976) (3).

La relación entre el uso de drogas y la experiencia migratoria de los estudiantes pueden estar indicando que el movimiento migratorio que ha caracterizado a la población puertorriqueña durante los últimos años, además de estar afectando la estructura poblacional de la Isla, está haciéndose sentir en los patrones de conducta en esta sociedad.

Una de las características más sobresalientes de la estructura poblacional de Puerto Rico

en los últimos diez años es la gran cantidad de personas que están regresando a la Isla después de haber vivido por varios años en Estados Unidos. Según los datos del Censo del 1970, más de 225,000 puertorriqueños regresaron de Estados Unidos entre los años 1965 al 1970 (U.S. Bureau of the Census, 1970) (4). Las estadísticas del Departamento del Trabajo indican que en los últimos cinco años la cantidad de puertorriqueños que habían regresado de Estados Unidos ascendió a 92,731 individuos (San Juan Star, September 21, 1976) (5).

Para tener un cuadro más completo de los procesos migratorios de Puerto Rico es importante señalar que alrededor de 16,035 habitantes de las Islas Vírgenes y 15,548 de otros países también se incorporaron a la población de Puerto Rico durante el pasado año fiscal (San Juan Star, September 21, 1976) (5).

Las características y magnitud del movimiento migratorio en la sociedad puertorriqueña y los hallazgos de este estudio relativos a la experiencia migratoria hacen necesario definir más específicamente aquellos factores de esta experiencia que están relacionados con el uso de drogas entre los adolescentes.

Entre ambos sistemas escolares se manifiesta una diferencia clara entre las percepciones de salud y felicidad que tienen los estudiantes que usan alcohol. Este dato nuevamente sugiere que los estilos de vida de los diferentes grupos socioeconómicos a que pertenecen los estudiantes pueden estar influenciando el significado

que se le atribuye al uso de alcohol en ambos grupos de adolescentes.

La frecuencia de uso tanto de drogas lícitas como ilícitas es más alta en las escuelas privadas. El grupo con mayor frecuencia de uso de ambos tipos de drogas son los varones de las escuelas privadas. En frecuencia de uso de drogas ilícitas le siguen sus pares del mismo sexo de las escuelas públicas. En uso de alcohol le siguen las hembras de las escuelas privadas.

Los estudiantes que usan drogas ilícitas tienden a percibirse con salud más pobre e infelices. También tienen notas más bajas, han tenido experiencia migratoria y tienden a asociarse con otros adolescentes que también usan drogas.

## RECONOCIMIENTO

Deseamos agradecer el interés y la ayuda brindada por el Dr. Luis A. López y el Dr. José E. Sifontes del Recinto de Ciencias Médicas.

## REFERENCIAS

1. Josephson, E.: Addictive Diseases, an International Journal 1 (10): 55, 1974
2. Johnston, L.: Drugs and American Youth, Institute for Social Research, Ann Arbor, Michigan, 1973.
3. Kandel, D., Single, E., Kessler, R.: American Journal of Public Health 66: 43, 1976.
4. U. S. Bureau of the Census: Population Census: Puerto Rico, 1970.
5. San Juan Star, September 21, 1976, p. 3.

# THE SAFETY OF PERCUTANEOUS ARTERIOGRAPHY: INDICATIONS, TECHNIQUES AND RESULTS

R. García Rinaldi, MD, Ph.D., C. H. McCollum, MD, J. M. Graham, MD,  
W.W. Defore, MD, and M. E. DeBakey, MD.

Successful arterial reconstructive surgery requires precise definition of the occlusive or aneurysmal process and the condition of the vessels in the distal vascular tree. To define these two parameters it is essential that arteriography be precise. However, arteriography must also be safe, reproducible, and painless.

A recent manuscript has emphasized the frequency with which vascular trauma results when arteriography is performed utilizing percutaneous catheter techniques (1). At our institutions, we continue to utilize percutaneous arteriography without catheters because of its safety and excellent delineation of the vascular system (2). The purpose of this paper is to discuss the indications, techniques, and results of percutaneous arteriography for the evaluation of peripheral atherosclerotic arterial disease.

## CLINICAL MATERIAL

During 1975, a total of 1,253 percuta-

neous arteriograms were performed at The Cardiovascular Research Center of The Methodist Hospital in Houston, Texas.

On admission, all patients received a thorough history and physical examination with particular emphasis on symptoms related to angina, claudication, transient ischemic episodes, post prandial abdominal pain, and the presence of pulsatile masses. A history of allergy to dyes or drugs was carefully sought. All peripheral pulses were felt, the blood pressure recorded, and peripheral arteries auscultated. Routine chest and abdominal films were obtained. The clotting time, prothrombin time, partial thromboplastin times and platelet counts were determined. Coumadin anticoagulation was reversed with Aqua Mephyton ® given on the day of admission. Before arteriography, the desired prothrombin time activity must be at least 80 percent of normal to minimize the formation of hematomas or prolonged bleeding from the puncture site.

## PRE-ARTERIOGRAM PREPARATION

Patients were given a sedative the evening prior to arteriography. Before beginning the procedure the patients received 0.6 mg atropine intravenously. Patients with a known allergy to dye received 100 mg Benadryl ® and 250 mg Methylprednisolone (Solu Medrol ® ) given intravenously on arrival at the arteriography suite. After this preparation, most patients

---

*From the Cora & Webb Mading Department of Surgery, Baylor College of Medicine, Houston, Texas.*

*Reprint requests: Raúl García-Rinaldi, MD, PhD, Cora & Webb Mading Department of Surgery, Baylor College of Medicine, 1200 Moursund Avenue, Houston, Texas 77030.*



have no reaction from a test dose of the contrast material given intravenously, and experience no difficulty with intra-arterial injection of the contrast material.

All arteriograms were done under general anesthesia. An intravenous solution of 5 percent Dextrose in Ringer's lactate was given to all patients. Anesthetic induction was with sodium thiopental and relaxation was accomplished with succinyl choline. In patients undergoing carotid arteriography, a cuffed endotracheal tube was inserted. In all other patients, ventilation was done with a mask without intubation. Maintenance anesthesia consisted of nitrous oxide and oxygen.

## TECHNIQUES

### CAROTID ARTERIOGRAPHY

We perform carotid arteriography for patients who present with transient ischemic episodes, or a previous cerebrovascular accident (CVA). We also perform carotid arteriography in any patient who has a carotid bruit discovered during the preoperative evaluation of other cardiovascular disease. Our policy is to perform carotid endarterectomy prior to other cardiovascular procedures in patients with both conditions.

The patient is anesthetized and an oral endotracheal tube inserted (Figure 1-A). After induction, the neck is prepped with Betadine® solution and the patient placed in a supine position with the neck hyperextended over a small roll beneath the scapula. The carotid artery is palpated and stabilized by applying pressure against the lateral aspect of the trachea, (Figure 1-B) or by holding the artery between the thumb and index finger of the left hand (Figure 1-C) so that it can be safely punctured. A Cournard needle (2 3/64, 18 gauge) is inserted into both carotid arteries 2 cm above the upper edge of the clavicle (Figure 1-B). The needle is inserted and both the anterior and posterior walls of the vessel can be pierced (Figure 2-A). The stylet of the

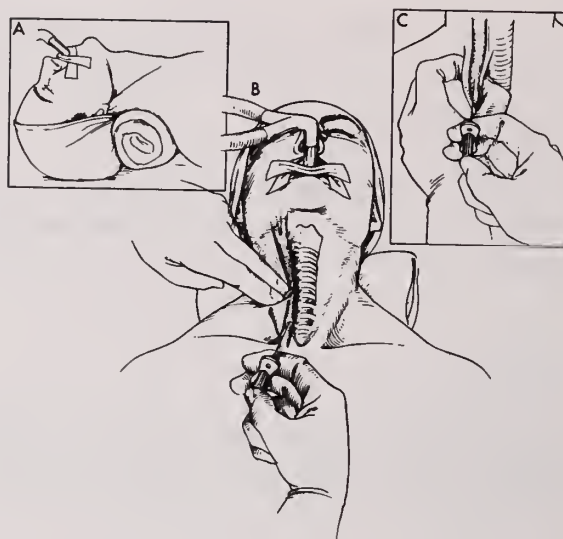


Figure 1: Carotid arteriography: A) a cuffed endotracheal tube is inserted and a roll placed behind the patient's neck. B) the artery is fixed by compressing medially against the trachea or c) the artery is fixed by holding it between the thumb and index finger of the left hand.

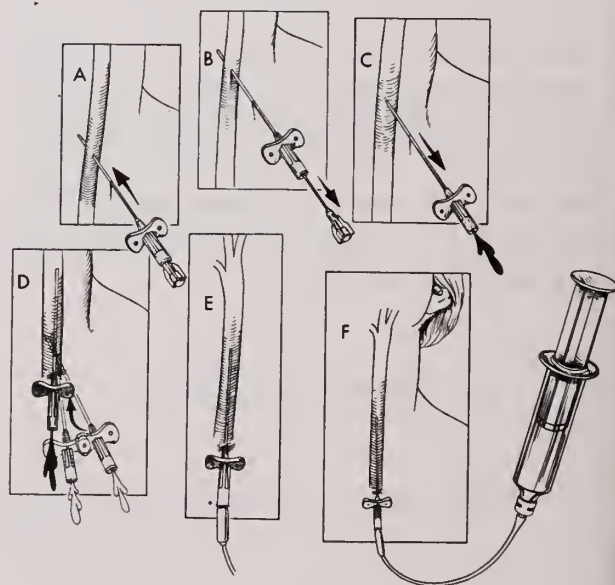


Figure 2: Carotid arteriography: Technique of puncture: Both anterior and posterior walls of the artery are pierced (A, B) the stylet is removed and the needle withdrawn until forceful backflow is observed (C) the Cournard needle is then advanced into the artery.

Cournard needle is removed and the needle withdrawn until a strong pulsatile backflow is observed indicating that the needle is now in the lumen of the artery (Figure 2 B, C). The needle is advanced into the artery (Figure 2-D). Alternatively, the puncture of the carotid artery can be performed by just piercing the anterior vessel wall and after insuring adequate backflow, the Cournard needle is advanced (Figure 3). The method of puncture selected depends on the experience of the operator. A 35 cc syringe with a 40 inch IV tubing extension is filled with 12 cc of sodium diatrizoate (Hypaque 50 percent ®). The opaque medium is rapidly injected to produce a bolus effect by hand injection. X-ray exposure is done when 3-5 cc of fluid remains in the syringe. Lateral views of the carotid artery and bifurcation with visualization of the intra-cranial arteries are taken. Anterio-posterior views are obtained when indicated.

The stylet is replaced and the films developed. If adequate delineation of the lesion and the distal vessel has been obtained, the procedure is repeated on the contralateral carotid artery. After satisfactory arteriograms have been obtained, the needles are removed one at a time, and the puncture site compressed for five minutes for hemostasis.

In different patients, the moment of exposure of the x-ray film may be varied, to allow different degrees of distal filling and opaque concentration. Figure 4 demonstrates an example of bilateral carotid arteriograms. Note the excellent delineation of the occlusive process.

#### VERTEBRAL ARTERIOGRAPHY BY RETROGRADE BRACHIAL INJECTION

We perform retrograde brachial arteriograms to visualize the subclavian and vertebral arteries on patients with symptoms of vertebral basilar insufficiency, and on patients with bruits over the subclavian artery.

Excellent visualization of the vertebral

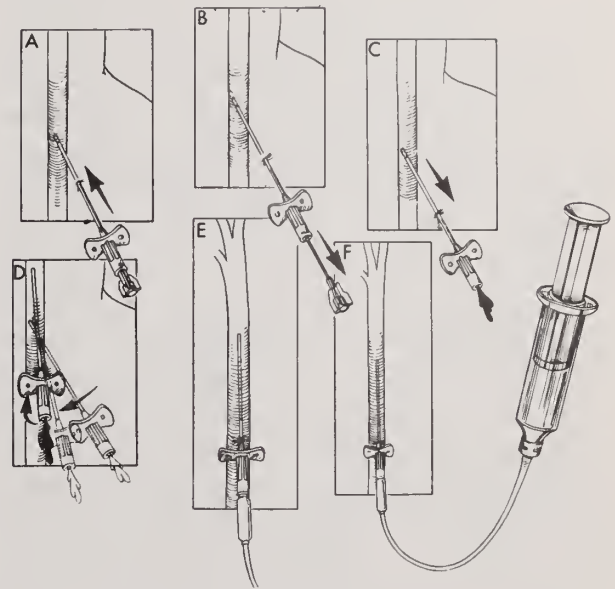


Figure 3: Carotid arteriography: Technique of puncture: only the anterior wall of the artery is pierced (A) the stylet is removed and when backflow is observed (B, C) the needle is advanced (D).



Figure 4: Percutaneous carotid arteriography: Note the precise delineation of the occlusive process that can be obtained.

and subclavian arteries can be obtained utilizing retrograde brachial arteriography and the complications of supra or subclavicular puncture are completely eliminated.

For the study of the vertebral-basilar system, the patient is placed in the supine position (Figure 5). The antecubital fossae are prepped with Betadine and a Cournard needle (2 3/64 inch, 18 gauge) inserted into each brachial artery utilizing one of the puncture techniques described under carotid arteriography. The needle stylet is removed and the needle withdrawn until good pulsatile flow is obtained. A 50 cc syringe and connective tubing are filled with 30 cc of Hypaque 50 ®. The syringe and tubing are connected to the needle and the dye injected manually utilizing maximum pressure. Exposure is done when 8-10 cc of opaque medium remain in the syringe. The stylet is replaced and the film developed. If the timing is inadequate, a re-injection can be safely done, adjusting the time of exposure to obtain greater proximal concentration of opaque medium. After an adequate film is obtained, the contralateral side is performed utilizing the same technique. Both arterial needles are removed and compression applied to the puncture sites to accomplish hemostasis. Figure 6 illustrates the excellent visualization of the vertebral arteries obtained by retrograde brachial artery injection.

### TRANSLUMBAR AORTOGRAPHY

We perform translumbar aortography for patients who present with ischemia of the lower extremities or intermittent claudication. Translumbar aortography is also used in some cases of abdominal aortic aneurysms, particularly when there is a question of supra-renal aneurysmal involvement, consideration of renal artery stenosis, or associated aorta-iliac or femoral occlusive disease.

The patient is ventilated by mask while lying in the prone position. Very adequate ventilation is possible and the weight of the head favors the easy application of the mask over the face (Figure 7). The x-ray table is constructed over an "x-ray Cassette Tunnel" (Figure 7). This is a rectangular box, housing a 14x36 inch film plate and a sliding lead shield. The shield

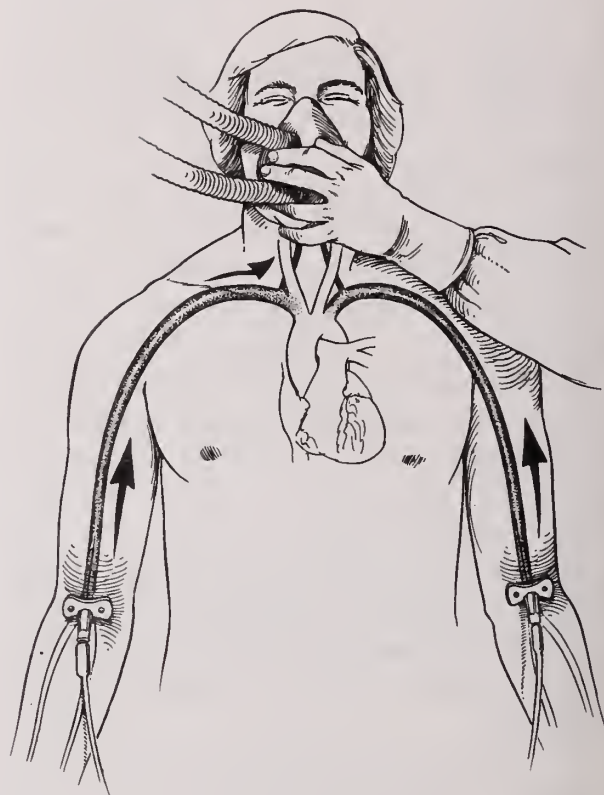


Figure 5: Vertebral and subclavian arteriography by retrograde brachial injection: with the patient supine and ventilated by mask, both brachial arteries are cannulated. The opaque medium is forcefully injected in a retrograde manner.

can be moved up or down to cover the segment of x-ray film underlying the abdomen or the lower extremities.

The patient's left flank is prepped with Betadine solution and draped. A 50 cc syringe is filled with 45 cc of (Angio-Conray 80 ®). A thin-walled, 7 inch 17 gauge aortogram needle is inserted at a point under the 12th rib and just lateral to the paraspinal muscles, at a 45° angle and aimed at the right axilla (Figure 8-A). Frequently, the needle will hit a vertebral body. Repositioning the needle in a more lateral direction will usually locate the aorta (Figure 8-C).





Figure 6: Retrograde bilateral brachial arteriography: observe the clear definition of the vertebral arteries.

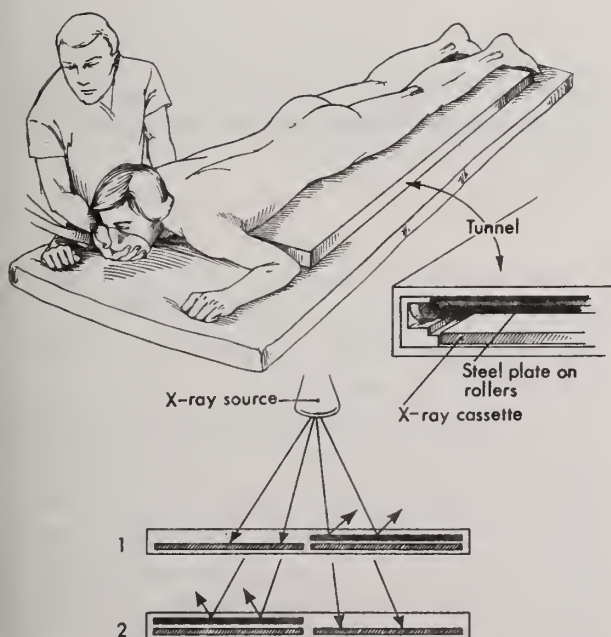


Figure 7: Translumbar aortography: The patient is prone, ventilated by mask. The x-ray table is constructed so that a movable steel plate covers one half of the x-ray cassette. By moving the steel plate the proximal and then distal portions of the x-ray cassette are exposed as the dye travels distally in the vascular system.

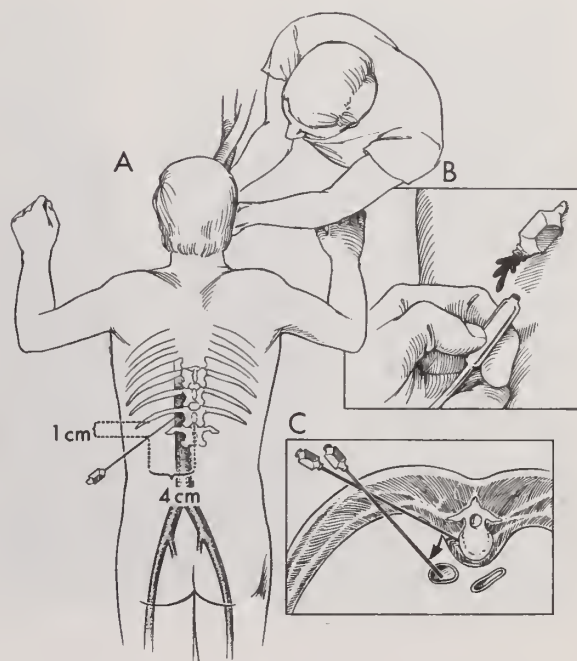


Figure 8: Translumbar aortography: The needle is inserted 4 cm to the left of the midline and 1 cm below the 12th rib.

of the needle with force to make sure that the needle is within the aortic lumen and prevent subintimal injections (Figure 8-B). The syringe and tubing with the dye are attached to the needle. The dye is injected manually utilizing maximum pressure. The proximal exposure is made when about 10 cc of dye remains in the syringe. After the initial exposure, the lead shield is quickly pulled up to the proximal position corresponding to the abdomen. This maneuver exposes the lower part of the x-ray. The operator then calls for the second exposure, the timing depending upon the status of the femoral pulses. The second exposure is made three to six seconds after the syringe is empty. The second exposure is performed to visualize the distal arterial runoff. The film is developed and repeated if timing is improper. If a subintimal injection has been made, the procedure is discontinued and repeated on the following day.

The aorta is usually entered at the level of the 12th thoracic or 1st lumbar vertebra. The stylet is removed. Blood should come out

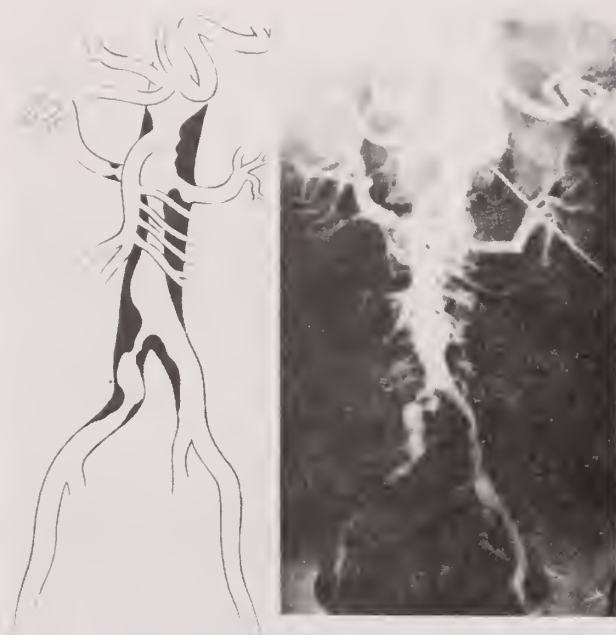


Figure 9: Translumbar aortography: note the severe occlusive disease of the entire abdominal aorta, the renal arteries and the iliac arteries.

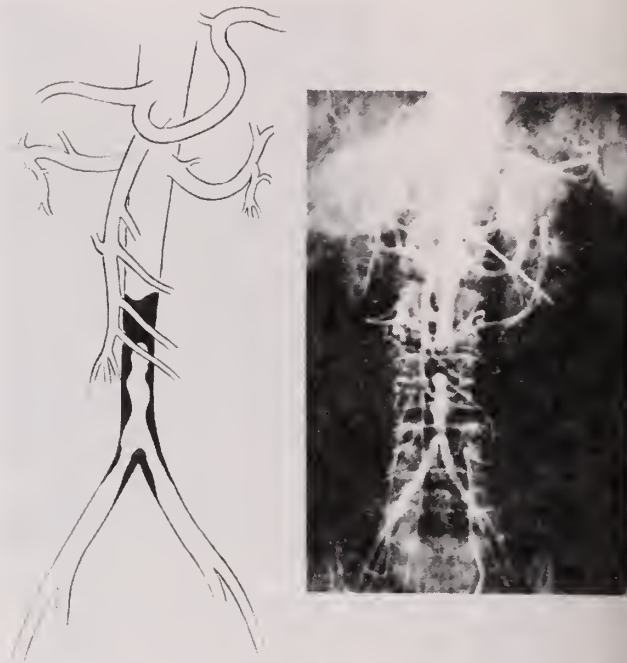


Figure 10: Translumbar aortography: there is complete occlusion of the abdominal aorta and stenosis of the proximal iliac arteries.

After an adequate film is obtained, the needle is removed and the patient immediately turned to the supine position. The patient is returned to the recovery room, is sedated and maintained at rest for the following 6-8 hours. The pulses and blood pressure are frequently checked and the urine output is recorded. Figures 9 and 10 illustrate the sharp delineation of the abdominal aorta and its branches obtained with a translumbar aortogram.

### FEMORAL ARTERIOGRAPHY

We perform femoral arteriograms in patients with ischemia of the feet and/or intermittent claudication who have absent popliteal or pedal pulses.

Femoral arteriograms are performed either singly or after aortography, to evaluate the femoral, popliteal, and distal shank arteries. Infrequently, excellent visualization of the

femoral and tibial vessels is obtained at the time of aortography, and a separate femoral arteriogram is not required.

Ventilation is performed utilizing a mask while the patient is supine on the x-ray table (Figure 11). The groins are prepped with Beta-dine and a 2 3/64 inch, an 18 gauge Cournard needle is inserted into each common femoral artery (Figure 11). After proper intraluminal placement, two 35 cc syringes and plastic tubing connectors are filled with 30 cc of Hypaque 50 ® and connected to the needles. The technician is alerted and the lead shield pulled down to the distal position of the "tunnel". The right and left femoral arteriograms are done simultaneously, injecting the dye with maximal force manually. The first exposure is done when 10 cc of dye remain in the syringe. The lead shield is rapidly pulled to the proximal position of the tunnel and the second film taken 2-8 seconds completing the injection

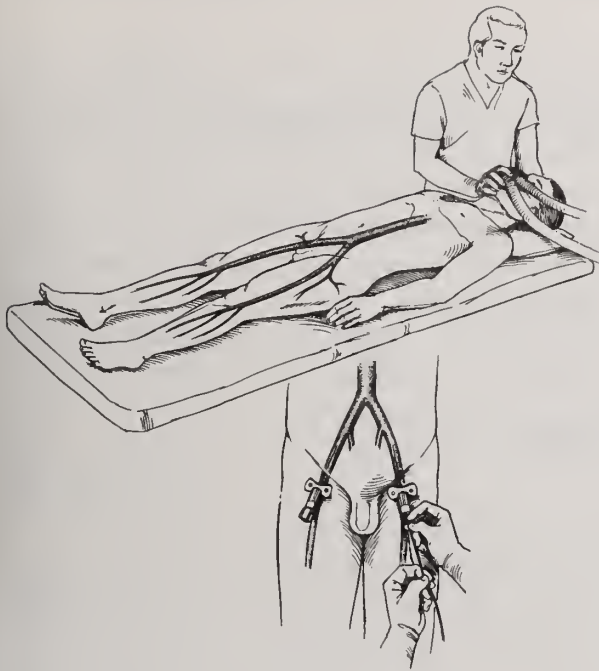


Figure 11: Femoral arteriography: Ventilation is done by mask. After cannulation of the femoral arteries, both are injected simultaneously.



Figure 12: Femoral arteriography: Note the bilateral superficial femoral artery blocks and the excellent visualization of the distal popliteal artery and shank vessels.

of the dye. As stated above, the timing sequence may vary according to the expected occlusive disease process. The film is developed and repeated if necessary. After good quality films are obtained, the needles are removed and manual pressure applied for five minutes for hemostasis. The patient is returned to the recovery room and sedated. The groins are observed for the formation of hematomas, and any change in the distal circulation or pulse status observed. Figure 12 demonstrates the excellent visualization obtained by bilateral percutaneous femoral arteriography. The shank vessels opacify well.

## RESULTS

During the year 1975, 1,253 arteriograms were performed. Table I lists the number of each of the procedures done. Six patients (0.5 percent) had a history of allergy to dye.

Each was given 250 mg Solu Medrol ® IV and 100 mg of Benadryl ® prior to induction of anesthesia and in all, an endotracheal tube was inserted. The EKG was monitored in all patients. Cardiotonic medications were kept in the arteriography room. None of the patients had any untoward effects.

Nine patients (0.7 percent) developed complications. None of the complications resulted in death of any of the patients, although four of them were life-threatening. Two patients developed congestive heart failure shortly after the procedure. These patients responded to digitalization and diuresis. Two patients developed cervical hematomas and airway obstruction. They were reintubated and remained with the endotracheal tube until the hematoma was drained in one and an endarterectomy and dacron patch angioplasty was performed on the other. One patient who vomited in the prone position was immediately turned to the supine



TABLE I

<i>Aortogram</i>	225
<i>Aortogram and femoral arteriogram</i>	329
<i>Aortogram and femoral and carotid and vertebral (retrograde brachial) arteriogram</i>	38
<i>Femoral arteriograms</i>	147
<i>Femoral and carotid and/or vertebral (retrograde brachial) arteriograms</i>	26
<i>Carotid arteriogram</i>	251
<i>Vertebral (retrograde brachial) arteriogram</i>	15
<i>Carotid and vertebral (retrograde brachial) arteriogram</i>	175
	1253

TABLE II

1. <i>Hypotension on induction</i>	1
2. <i>Rupture of endotracheal tube cuff</i>	1
3. <i>Respiratory problems:</i>	
a. <i>Prolonged apnea after succinyl choline</i>	1
b. <i>Bronchospasm</i>	1
4. <i>Congestive heart failure</i>	2
5. <i>Cervical hematoma with airway obstruction</i>	2
6. <i>Vomiting in the prone position</i>	1
<i>TOTAL</i>	9

position, suctioned and intubated. He had no further complications.

One patient's endotracheal tube cuff ruptured while the arteriogram was being made. The tube was immediately replaced without complications.

One patient remained apneic for 3 hours after receiving succinyl choline. Ventilation

was maintained with a mechanical respirator. One patient (non-allergic) developed bronchospasm after the arteriogram. He responded to adrenalin and aminophylline given intravenously.

## DISCUSSION

Percutaneous arteriography allows excel-

lent visualization of the vascular system. By following the precautions outlined: i.e. avoidance of subintimal injections, adequate ventilatory support and careful follow-up of the patient in the postarteriogram period, complications can be avoided. By a careful preoperative evaluation, allergic patients can be identified and medications administered to prevent catastrophic accidents at the time of arteriography. By a careful history and physical examination, patients on anti-coagulants can be identified and treated.

We prefer to perform arteriography under general anesthesia. Besides avoiding pain and apprehension for the patient, any complication which may arise is easily treated with the patient asleep. However, should general anesthesia be contraindicated, the procedures outlined here can be safely adapted to local anesthesia.

We believe arteriography should be performed by a member of the surgical team. This is the person who can most accurately correlate the arteriographic findings with the clinical

picture. It is the members of the surgical team who can best judge if the quality of the films obtained is good enough to base the patient's operation on the particular set of x-rays. This does not imply that the participation of a radiologist is not encouraged. The radiologist should be a member of the arteriography team rather than the one making the decisions regarding the type of films that the patients need and the quality of x-ray acceptable before undertaking vascular reconstruction.

## REFERENCES

1. Rich, Norman M., Hobson II, Robert W., and Fedde, C. W.: Vascular Trauma Secondary to Diagnostic and Therapeutic Procedure. *Am. J. Surg.* 128: 715, 1974.
2. Beall, A. C., Lewis, J. M., Weibel, J., Crawford, E. S., DeBakey, M. D.: Angiographic Evaluation of the Vascular Surgery Patient *Surg. Clinics of North America* 46: 843, 1966.

## CORONARY ARTERY ANEURYSM: CASE REPORT WITH REVIEW OF LITERATURE

Rafael A. Cox, MD, Pablo I. Altieri, MD, Fernando Martínez Catinchi, MD  
and Félix I. León Rivero, MD

**Summary:** We have reported a case of coronary artery aneurysm in a patient with severe aortic insufficiency. The functional and anatomical features were fully elucidated by cardiac catheterization and selective coronary angiography.

This uncommon cardiac disorder may be of congenital or of acquired origin. Congenital aneurysms should be suspected when myocardial infarctions occur in young people. The acquired aneurysms are usually secondary to atherosclerosis but can also have a traumatic or inflammatory origin. Both in the congenital and acquired varieties right coronary artery involvement has been more frequently reported. Some cases have presented a generalized aneurysmal dilatation of the main coronary arteries instead of having distinct aneurysmal lesions. For these cases the term coronary ectasia is more appropriate and the lesion has usually an atherosclerotic origin.

Since 1971 these lesions have been successfully treated with surgery by various authors. Chronic anticoagulation has been recommended for those who will receive just medical therapy. Medical treatment was elected in the case just reported in view of the extensive involvement of his coronary tree, a poor distal run-off and a depressed ventricular function.

**Resumen:** Se reporta un caso de aneurismas de las arterias coronarias en un paciente con insuficiencia aórtica severa. El diagnóstico se hizo mediante el cateterismo cardíaco y la angiografía selectiva de las arterias coronarias.

Esta lesión cardíaca es poco frecuente y puede ser de origen congénito o adquirido. Los aneurismas congénitos se deben sospechar ante un paciente joven que presenta un cuadro de infarto agudo del miocardio. Los aneurismas adquiridos están más comunmente asociados a arteriosclerosis, pero pueden también deberse a trauma o a lesiones inflamatorias. Tanto en los casos congénitos como en los adquiridos, la arteria coronaria más frecuentemente afectada es la coronaria derecha. Algunos casos no presentan lesiones aneurismáticas circunscritas, sino que lo que se vé es una dilatación generalizada de la luz de los vasos coronarios. Para estos casos se reserva el término de ectasia de las arterias coronarias; esta lesión es usualmente secundaria a arteriosclerosis.

Desde el año 1971 se han reportado varios casos que han tenido un tratamiento quirúrgico exitoso. En los casos en que se elija el tratamiento médico solamente, se recomienda la anticoagulación crónica. En el caso que reportamos aquí se eligió el tratamiento médico debido a la extensión de las lesiones aneurismáticas con un flujo distal pobre y a la depresión de la función ventricular izquierda.

---

*From the Cardiology Section, Department of Medicine, University District Hospital, University of Puerto Rico School of Medicine, San Juan, Puerto Rico.*

*Reprints requests to Dr. R. A. Cox, Cardiovascular Laboratory, University District Hospital, San Juan, Puerto Rico 00936.*

The first report of a coronary artery aneu-



rysm in the world medical literature is credited to Bougon in 1812 (1). However among the brilliant pathologic observations in "De sedibus et causis morborum per anatomen indagatis" (1761), Morgagni reported a case of luetic aortitis which at the same time had greatly dilated coronary arteries (2). Since then multiple reports of this condition have appeared in the literature. However, few of these cases have been diagnosed during life.

We report a case in which the diagnosis was made by selective coronary angiography in a patient with severe aortic insufficiency and persistent angina pectoris. To our knowledge only one previous report of this condition has appeared in the medical literature of Puerto Rico; it consisted of two cases diagnosed post-mortem (3).

### CASE REPORT

The patient, a 61 year-old Caucasian male was referred for evaluation to our center because of a three year history of progressive angina pectoris. He had had multiple hospital admissions elsewhere due to this problem. However, he never had documented evidence of an acute myocardial infarction. Lately he had been having angina with minimal effort and angina decubitus. His treatment consisted of digoxin, propranolol and nitrates.

His past medical history was negative regarding diabetes mellitus, arterial hypertension, hyperlipidemia, venereal diseases, rheumatic fever or chest trauma.

On physical examination he had a blood pressure of 180/50, a pulse of 48 beats per minute, bounding and regular. His lungs were clear. The examination of the heart disclosed a grade 2/6 ejection systolic murmur at the base and the apex, a grade 3/6 early diastolic decrescendo murmur along the left sternal border and a diminished aortic component of the second sound.

The resting electrocardiogram showed sinus bradycardia and left ventricular enlargement. The chamber analysis disclosed cardiomegaly with left ventri-



Figure 1: Selective angiography of the left coronary artery showing aneurysmal dilatation of the proximal third of the left anterior descending branch (arrow) with diminished caliber of its distal two-thirds.



Figure 2: Right coronary angiogram showing aneurysmal dilatation in its initial and mid-portions (see interrupted lines).

cular enlargement and a dilated ascending and descending aorta with calcified aortic knob. The laboratory investigations revealed hypercholesterolemia but no evidence of diabetes mellitus or lues.

The patient was submitted to cardiac catheterization which revealed severe aortic insufficiency. Selective coronary angiography (figures 1-2) disclosed aneurysmal dilatation of the proximal third of the

left anterior descending coronary artery with very small caliber of its distal two thirds. It also showed multiple aneurysms all along the right coronary artery. The left ventriculogram showed a ventricle with depressed ejection fraction but no akinetic areas. The decrease in ejection fraction was due to reduction in segmental wall motion in the anterior, apical, inferior and infero-basal segments.

After extensive discussion it was decided to treat him medically because the multiple aneurysms in the right coronary artery involved all its branches and it was not possible to insert a graft. In the left coronary artery the distal run off was inadequate. Aortic valve replacement was considered too risky in this setting.

## DISCUSSION

Coronary artery aneurysms are a rare finding. Packard and Wechsler (4) in 1929 made the first extensive review of the literature, collecting twenty nine cases previously reported and adding one case of their own. Reviews of the available literature were subsequently done by Scott (5) in 1948, Crocker et al (6) in 1957 and Daoud et al (7) in 1963. In 1958 Munkner et al (8) diagnosed the first case in which the functional and anatomical features were fully elucidated by cardiac catheterization and angiocardiology. In 1971 Ebert et al (9) described the fifth patient diagnosed during life and the first one to be operated on by saphenous vein graft. Subsequently there have been various cases diagnosed which have been submitted to cardiac surgery (10), (11), (12) (13).

The aneurysms or ectasia of the coronary arteries have been found as isolated congenital lesions or in association with congenital heart disease, scleroderma, periarteritis nodosa, Ehlers-Danlos syndrome, bacterial endocarditis, lues and atherosclerosis.

For the purpose of this discussion these lesions will be divided into two large groups (See table): those of congenital and those of

TABLE I

### *Classification of coronary artery aneurysm*

#### *I Distinct coronary artery aneurysm*

##### *A. Congenital*

- 1. Isolated*
- 2. Associated to other conditions*

##### *B. Acquired*

- 1. Atherosclerotic*
- 2. Inflammatory*
- 3. Traumatic*

#### *II Coronary artery ectasia*

acquired origin.

The congenital coronary aneurysms have been reported as isolated lesions (14, 15) and associated with coronary arteriovenous fistula (8, 16). The most common site of single congenital coronary artery aneurysm has been found to be the right coronary artery. Their reported incidence varies. In Scott's collection of forty-seven cases most of the cases were congenital. He also suggested that many coronary aneurysms considered to be atherosclerotic were in fact congenital with secondary atherosclerotic changes. Congenital aneurysms of the coronary arteries can be suspected when myocardial infarction or angina pectoris occurs in a young person. Myocardial infarction occurs because of thrombosis of the aneurysm; commonly too, embolization of a small thrombus within the aneurysm causes occlusion of distal coronary artery branches.

The acquired coronary artery aneurysms may be atherosclerotic, inflammatory or secondary to trauma. In Daoud's review of eighty-nine cases of coronary artery aneurysms fifty two percent were found to be atherosclerotic versus seventeen percent congenital, eleven percent mycotic-embolic and four percent luetic. In most reported series involvement

of the right coronary artery, by localized aneurysm, has been more commonly found than involvement of the left coronary. The development of the atherosclerotic coronary aneurysm is felt to be due to destruction of the musculoelastic elements in the media by the extension of the atherosclerotic process from the intima. There have been an impressive association between the atherosclerotic coronary aneurysms and the presence of concomitant abdominal aortic aneurysms in the reported cases. There have been no available clues as to the presence of the coronary aneurysm prior to death or to coronary angiography. Few reports have described radiographically visible calcifications in these lesions (3, 16).

The inflammatory type of coronary artery aneurysm has been more frequently associated with periarteritis nodosa. Other reported cases have been associated with bacterial endocarditis, lues and rheumatic carditis.

Coronary artery aneurysm may also be found in patients with penetrating trauma to the chest and heart as well as nonpenetrating chest trauma (12). The way in which the aneurysm develops may vary. Some have described first a dissection of the coronary artery with weakening of its wall and eventual formation of a false aneurysm. Traumatic coronary artery aneurysm have been usually associated with extensive myocardial damage.

There have been some cases which instead of having distinct aneurysmatic lesions in the coronary vasculature, present a generalized aneurysmal dilatation of the main coronary arteries with or without any obstructive lesions, for which the term ectasis has been variously employed. The nature of the coronary artery disease is felt to be atherosclerotic in most of these cases. In a recent report of this subject Markis et al (17) comment that the prognosis of this lesion is the same as for the patients with three vessel obstructive coronary artery disease treated medically. Surgery has

been tried in some patients with improvement of symptoms. Death in these cases have been attributed to sudden rupture of the aneurysm, myocardial infarction or unavailability of treatment. It has been recommended that if medical therapy is elected these patients should receive anticoagulation indefinitely.

## REFERENCES

1. Bougon: Bibl. Med. 37: 183, 1812. Cited by Packard M., Wechsler, H. F.: Aneurysm of coronary arteries. Arch Intern Med: 43: 1, 1929.
2. Morgagni, J. B.: De sedibus, et causis morborum per anatomen indagatis. Tomus primus, Liber II, Epist 27, Article 28 Venetiis, 1761.
3. Ramírez, E. A., Taveras, J. E., Haddock, J.: Arteriosclerotic aneurysm of the cardiac coronary arteries. Bol Asoc. Med. Puerto Rico 51: 268-280, 1959.
4. Packard, M., Wechsler, H. F.: Aneurysm of coronary arteries. Arch Intern Med: 43: 1, 1929.
5. Scott, D. H.: Aneurysm of coronary arteries. Am Heart J 36: 403, 1948.
6. Crocker, D. W., Sobin S., Thomas, W. C.: Aneurysms of the coronary arteries: Report of three cases and review of the literature. Am J Path 33: 819, 1957.
7. Daoud, A. S., Pankin, D., Tulgan, H., et al: Aneurysm of the coronary artery; report of ten cases and review of the literature. Am J Cardiol 11: 228, 1963.
8. Munker, T., Petersen, O., Vesterdal, J.: Congenital aneurysm of the coronary artery with arteriovenous fistula. Acta Radiol 50: 333, 1958.
9. Ebert, P. A., Peter, R. H., Gunnels, J. C., et al: Resecting and grafting of coronary artery aneurysm. Circulation 43: 593, 1971.
10. Mattern, A. L., Baker, W. P., McIlale, J. J., et al: Congenital coronary aneurysms with angina pectoris and myocardial infarction treated with saphenous vein bypass graft. Am J Cardiol 30: 906, 1972.
11. Ghahramani, A., Iyengar, R., Cunha, D., et al: Myocardial infarction due to congenital coronary aneurysm (with successful saphenous vein bypass graft). Am J Cardiol 29: 863, 1972.
12. Cheng, T. O., Adkins, P. C.: Traumatic aneurysm of the left anterior descending coronary artery with fistulous opening into the left ventricle and left ventricular aneurysm after stab wound of chest, report of a successful surgical repair. Am J Cardiol 31: 384, 1973.
13. Razavi, M.: Unusual forms of coronary artery disease, in Cleveland Clinic Cardiovascular Consultations, edited by Vigt, D. C., F. A. Davis Company, Philadelphia Vol. 7



- no. 1, pp 25-46, 1975.
11. Gore, I., Smith, J., Clancy, R.: Congenital aneurysms of the coronary arteries with report of a case. *Circulation* 19: 1959.
15. Grob, M., Kolb, E.: Coronary aneurysm with arteriovenous fistula. *Am Hear J* 48: 270, 1954.
16. Colbeck, J. C., Shaw, J. M.: Coronary aneurysm with arteriovenous fistula. *Am Hear J* 48: 270, 1954.
17. Markis, J. E., Joffe, C. D., Cohn, P.F., et al: Clinical significance of coronary arterial ectasia. *Am J Cardiol* 37: 217, 1976.

## NOTAS TERAPEUTICAS

### LAS PENICILINAS

Carlos H. Ramírez Ronda, MD, FACP, Carlos León Valiente, MD  
y Ramón H. Bermúdez, MD

Las penicilinas son los antibióticos más comunmente usados en la práctica diaria de la medicina. Son las penicilinas los antibióticos de mayor efectividad en el tratamiento del número mayor de enfermedades microbianas. Cuando hablamos de la penicilina tenemos que pensar en varios tipos, aunque la penicilina G o penicilina benzil es una de las formas más usadas y a lo que mayormente nos referimos cuando mencionamos penicilina. Para los propósitos didácticos discutiremos básicamente la farmacología de las diferentes penicilinas, penicilina G, penicilina V o fenoximetil penicilina; los derivados sintéticos de penicilina los cuales son resistentes a la degradación de penicilinasas como es la metilcilina y las penicilinas sintéticas con un espectro amplio incluyendo organismos gram negativos tales como son la ampicilina, amoxicilina y la carbenicilina.

#### PENICILINA G

##### Farmacología

La penicilina G tiene una absorción oral

pobre y solamente el 20 por ciento de la dosis se absorbe. Hay varias preparaciones de penicilina G entre las que se encuentran: a) Penicilina G sódica, la cual es altamente soluble y se administra endovenosamente; b) Penicilina G potásica, idéntica a la anterior pero en sal potásica; c) La penicilina G procainada, la cual es menos soluble y se administra intramuscularmente solamente y; d) La penicilina G benzatínica, la cual es la menos soluble y tiene una duración prolongada y se administra intramuscularmente. El 90 por ciento de la excreción es tubular y el 10 por ciento por filtración glomerular. El 70 por ciento de una dosis se excreta en la orina en forma no alterada en término de seis horas. La penetración a las vías biliares es pobre. Las penicilinas se inactivan en el hígado pero esta inactivación es usualmente menor de 10 por ciento. La distribución es esencialmente a todos los lugares del cuerpo, se difunden rápidamente a los espacios y líquidos pleurales, pericárdicos, ascíticos y sinoviales. La penetración al líquido cerebroespinal no es tan buena, pero cuando ocurre inflamación meníngea la penetración aumenta. La penetración a lugares avasculares y a abscesos es pobre, lo cual hace difícil el tratamiento de una infección dentro de un tejido avascular o un absceso. La penicilina penetra y cruza la placenta rápidamente.

##### Organismos Sensibles

Los organismos que son sensibles a la peni-

---

*De la Sección de Enfermedades Infecciosas, Departamentos de Investigación y Medicina, Hospital de Veteranos y Escuela de Medicina, Universidad de Puerto Rico, San Juan.*

*Favor de pedir reimpresos al Dr. Carlos H. Ramírez Ronda, VA Hospital (151), GPO Box 4867, San Juan, Puerto Rico 00936.*

cilina son muchos, entre los más comunes los cocos gram positivo tales como el estreptococo, el neumococo, los estreptococos anaeróbicos y el estreptococo del tipo viridans. Debemos de estar conscientes que el enterococo o *Streptococcus fecalis* son mucho menos sensibles a penicilina que los demás estreptococos. Tenemos que asumir que todos los estafilococos causando infección en un paciente son resistentes a penicilina. Los bacilos gram positivos como son los clostridios, *Corynebacterium diphtheriae*, *Bacillus anthrax* y *Listeria monocytogenes* son sensibles a la penicilina. Podemos decir que todos los bacilos gram negativos no son sensibles a la penicilina aunque se sabe que si la concentración de penicilina aumenta hasta 78 unidades por mililitro, hay algunos organismos gram negativos tales como *Escherichia coli* y *Proteus mirabilis*, los cuales son sensibles a estas concentraciones. Estas concentraciones se pueden obtener sin dificultad en la orina pero no en suero. Otro grupo de organismos los cuales son sensibles a la penicilina incluye el *Treponema pallidum*, agente causante de la sífilis y las leptospiros al igual que *Streptobacillus moniliformis*, *Spirillum minus* y *Actinomyces*.

### Dosificación

La dosificación de la penicilina es usualmente como sigue: Dosificación parenteral: a) Penicilina procainada, 600,000 a 1,200,000 unidades intramuscular al día; b) Penicilina G sódica se utiliza para obtener una concentración alta en suero en una dosificación de 10,000,000 a 20,000,000 unidades endovenosamente por día divididas en dosis no menos frecuentes que cada cuatro horas; c) Penicilina G benzatínica: 600,000 a 2,400,000 unidades intramuscular. Dosificación oral: Penicilina G usualmente 1 gramo antes de las comidas cada 6 horas o cuatro veces al día; d) Penicilina V, 250 mg a 500 mg antes de las comidas cuatro veces al día.

### Toxicidad

La toxicidad de las penicilinas se manifiesta usualmente por reacciones de hipersensitividad. Estas ocurren en el 2 por ciento al 8 por ciento de los individuos que se tratan con penicilina G o uno de sus derivados. Las reacciones alérgicas a penicilina pueden ser de varios tipos: a) anafiláctica, las cuales ocurren en términos de segundos a 30 minutos después de la administración de penicilina; b) aceleradas, que ocurren entre 30 minutos y 48 horas; c) tardías que ocurren de días a semanas después que se administra la penicilina. Aproximadamente una de mil de todas las reacciones son del tipo anafiláctico, y la muerte ocurre en el 5 por ciento al 10 por ciento de estas, particularmente cuando la penicilina se administra parenteralmente. Es imperativo por lo tanto que el médico pueda identificar estos individuos que son propensos a reaccionar a la penicilina de tal manera que pueda sustituirse un antibiótico alternativo. El mecanismo de alergia se debe a la sensitización por los derivados del ácido 6-aminopenicillánico uniéndose a las proteínas del cuerpo para formar compuestos antigénicos o haptenos. La manera para determinar si el paciente es verdaderamente alérgico a penicilina es muy difícil. Aunque un historial de alergia a penicilina es de gran ayuda no es una manera definitiva de estar seguro. Hay una gran mayoría de los pacientes que han tenido experiencia con una reacción alérgica a penicilina que pueden tolerar dosificación terapéutica de penicilina sin desarrollar efectos secundarios. El uso de la prueba de piel usando el derivado de polylysina de peniciloyl (PPL) para determinar los anticuerpos a peniciloyl, el cual es el producto de degradación principal de la penicilina y por lo tanto se le llama el determinante hapténico mayor, puede ser de ayuda en identificar aquellos pacientes que son hipersensibles a penicilina. Debemos saber sin embargo que esta prueba no es muy específica y solamente el 27 por ciento de los pacientes



con un historial negativo pero con una prueba de piel positiva a PPL y 4 por ciento de los pacientes con un historial positivo pero con una prueba negativa a PPL reaccionaron desfavorablemente cuando fueron expuestos nuevamente a penicilina; de la misma manera que el 0.5 por ciento de los pacientes que tenían un historial negativo y una prueba de piel negativa lo hicieron. Por lo tanto a pesar de que puede ser de beneficio clínico predecir la sensibilidad de un paciente, basado ya sea en el historial de una alergia previa a penicilina o en una prueba positiva PPL, esto puede excluir de tratamiento con penicilina muchos pacientes que se beneficiarían de terapia con esta droga sin tener reacción a ella. Nosotros recomendamos que cuando estos pacientes están seriamente enfermos con infecciones las cuales son mejor tratadas con penicilina tales como, endocarditis bacteriana, enterocócica o estafilocócica el uso de esta familia de antibióticos no está contraindicada, siempre y cuando se tomen las precauciones debidas. Por otro lado debemos estar conscientes que el tratar infecciones menos severas con derivados de penicilina o penicilina en un paciente con un historial positivo para alergia no debe de hacerse y deben utilizarse antibióticos alternos. Queremos enfatizar que la prueba de PPL es muy pobre para predecir las reacciones anafilácticas. Esto se debe a que estas reacciones usualmente son mediadas a través de anticuerpos específicos en contra de los productos menores hapténicos de penicilina los cuales no pueden detectarse con la prueba de PPL pero sí podrían determinarse por la prueba de piel para determinantes menores la cual está en etapa experimental y no para uso general. Cuando hay que utilizar la penicilina en caso de vida o muerte, en una situación donde la droga de elección es penicilina y el paciente es alérgico a ésta, el paciente debe de desensitizarse y esto debe de hacerse en una Unidad de Cuidado Intensivo Médico en donde existan las facilidades y el equipo para tratar anafilaxis de ocurrir esta. Es imprescindible si un paciente se va a desensitizar tener a la mano Epinefrina acuosa

en una solución de 1 en 1,000. Para detalles del método de desensitización se refiere a un artículo publicado por el Dr. Green en *Annals of Internal Medicine*, Vol. 67, Pag. 235, 1967. Todas las penicilinas irrespectivo de cual sea, pueden causar las reacciones de hipersensitividad que hemos descrito.

### Reacciones a Penicilina Procainada

La penicilina procainada nunca debe usarse endovenosamente ya que de usarse puede causar convulsiones, parálisis respiratoria y un cuadro de hipotensión abrupto y severo.

### Otras Reacciones

El paciente que se trata con penicilina para sífilis puede tener una reacción llamada la Reacción Herxheimer la cual se caracteriza por un episodio de fiebre y escalofrío severo después de recibir la penicilina y el cual se limita a sí mismo sin un tratamiento específico, otro que no sea de soporte y con agentes tales como salicilatos. Sabemos que hay otras reacciones a penicilina tales como la toxicidad de la penicilina en el sistema nervioso central. Para que esto ocurra usualmente el paciente está recibiendo dosis masivas de penicilina como por ejemplo: 100,000,000 unidades al día, a esta dosificación la concentración en el líquido cerebroespinal se llega a un nivel crítico el cual irrita al sistema nervioso central causando convulsiones. Usualmente cuando ocurre esto el paciente tiene daño renal previo. La nefropatía asociada con penicilina usualmente se ve cuando se usan dosis altas de penicilina y está directamente relacionado no solo a la dosificación sino a la duración del tratamiento. El cuadro clínico se manifiesta usualmente por fiebre y eosinofilia, erupciones en piel, albuminuria y un aumento en la urea nitrogenada de la sangre. El cuadro de la orina se caracteriza por hematuria y de hacerse una biopsia renal se encontraría nefritis intersticial. La penicilina también puede causar aunque en un por ciento bajo de los casos anemia hemolítica con una prueba de Coomb positiva;

los anticuerpos del tipo IgG reaccionan en contra de las células rojas las cuales están cubiertas por penicilina.

Entre las reacciones que pueden ocurrir con altas dosis de penicilina es intoxicación de cationes, por ejemplo la penicilina G potásica 1,000,000 de unidades contiene 1.5 mili equivalentes de potasio y 1,000,000 de unidades de penicilina G sódica contiene 1.7 mili equivalentes de sodio.

### Uso de Penicilina

El uso clínico de penicilina G es para el tratamiento de las infecciones causadas por los estreptococos usualmente faringitis estreptocócica, enfermedades estreptocócicas como erisipelas. Enfermedades del tracto respiratorio en adultos como la pulmonía, la sinusitis; el tratamiento de otitis media, meningitis bacteriana, endocarditis bacteriana, infecciones en el puerperio, infecciones causadas por los clostridios, tétano, antrax, difteria, gonorrea, sífilis, actinomicosis, leptospirosis, fiebre por mordida de rata y en el tratamiento profiláctico de fiebre reumática.

### Penicilina V

La penicilina V o la fenoximetil penicilina es una penicilina que comparada con la penicilina G es estable en un medio ácido y cuyo espectro y uso es idéntico a el de la penicilina G. La dosificación varía que con penicilina V se usan 250 a 500 mg cada 6 horas, preferiblemente una hora antes de las comidas. Su absorción es 40 por ciento de la dosis oral y tiene niveles séricos en 30 a 60 minutos. Su excreción, toxicidad y usos son idénticos a penicilina G.

## PENICILINAS SEMISINTÉTICAS DE AMPLIO ESPECTRO

### Ampicilina y Amoxicilina:

Estas penicilinas semisintéticas derivadas del núcleo de penicilina son estables en ácidos,

sensibles a penicilinasas y tienen un espectro antimicrobiano que cubre organismos gram negativos. Además cubren los organismos gram positivos al igual que la penicilina G. El espectro añade los bacilos gram negativos tales como *Escherichia coli*, *Proteus mirabilis*, *Salmonella* y *Shigella*. Tenemos que estar conscientes que *Enterobacter*, *Klebsiella*, *Citrobacter*, *Providencia* y *Pseudomonas* son resistentes. La resistencia de las bacterias gram negativas se desarrolla por la producción del enzimo beta lactamasa que destruye la droga. Diferentes organismos gram negativos sintetizan diferentes beta lactamasas. La dosificación de ampicilina por la vía oral es de 50 a 100 mg por kilogramo por día en cuatro dosis, usualmente 500 mg cada 6 horas. Por vía parenteral se puede utilizar de 8 a 20 gramos por día en dosis divididas cada 4-6 horas. La toxicidad de ampicilina además de la toxicidad de las penicilinas en general se caracteriza por las siguientes adiciones: 1) desarrollo de erupciones es común y hasta el 20 por ciento de los pacientes desarrollan una erupción macular que aparece de cuatro a cinco días después de comenzar la terapia. Estas erupciones son más comunes después de la administración oral y posiblemente no indican hipersensitividad a penicilina. Es interesante apuntar que el 95 por ciento de los pacientes que tienen Mononucleosis Infecciosa y reciben ampicilina desarrollan erupciones; 2) disturbios gastrointestinales tales como náusea y diarrea ocurren con ampicilina más no son de consecuencia mayor. La ampicilina y sus relacionados se utilizan en las siguientes infecciones: 1) infecciones del tracto urinario; 2) septicemia causada por organismos gram negativos los cuales sean sensibles; 3) fiebre tifoidea, en el tratamiento de los portadores; 4) shigelosis; 5) otitis media; 6) meningitis bacteriana; 7) infecciones por *Listeria monocytogenes*; 8) infecciones del tracto biliar como colangitis con organismos sensibles y; 9) enfermedades venéreas tales como gonorrea y granulomas inguinales.

### Amoxicilina:



La amoxicilina es otra penicilina semisintética con el mismo espectro de ampicilina. Tiene como ventaja que se absorbe mejor y tiene niveles más altos en sangre. *Hemophilus influenzae* es exquisitamente sensitivo a amoxicilina, más debemos de saber que las cepas de *Shigella* no son sensibles. La dosificación es esencialmente la misma de ampicilina, aunque puede utilizarse cada 8 horas por boca para infecciones no severas. En infecciones del oído medio se ha demostrado ser superior a ampicilina y se prevee que cuando el precio baje sustituya a la ampicilina como antibiótico de elección en estas infecciones.

#### Carbenicilina:

La carbenicilina es una penicilina semisintética con actividad en contra de *Pseudomonas aeruginosa*, *Proteus* positivo para indol y otras bacterias gram negativas. Tiene un uso específico en el tratamiento de pacientes que tengan infecciones causadas por *Pseudomonas aeruginosa*. Debemos de estar conscientes que se necesitan niveles de 50 a 60 microgramos por mililitro para inhibir la mayor parte de las cepas de *Pseudomonas aeruginosa* pero que muchas otras requieren niveles de 200 microgramos por mililitros. Otro uso de carbenicilina es en el tratamiento de septicemia en los pacientes que tienen neutropenia con contajes de neutrófilos de menos de 500 por centímetro cúbico en la sangre. La dosificación con Carbenicilina debe de ser alrededor de 5 gramos intravenoso cada 4 horas. No debe de utilizarse Carbenicilina o su derivado para tratamiento de infecciones del tracto urinario ya que el número de cepas que desarrolla resistencia aumenta.

#### Penicilinas Semisintéticas - Resistentes a Penicilinas

Las penicilinas semisintéticas derivadas del núcleo del penicilina, estables y activas en pre-

sencia de penicilinas, son un grupo de penicilinas muy importantes. Como ejemplo utilizaremos metilicina, la más conocida y usada. Los organismos que son sensibles a este grupo de penicilinas incluyen aquellos que están en el espectro de penicilina G, además tienen actividad en contra de los estafilococos resistentes a penicilina G. Debemos de estar conscientes que estas penicilinas semisintéticas no son tan efectivas como la penicilina G para el tratamiento de los organismos que son sensibles a la penicilina G. A pesar de que estas penicilinas no son hidrolizadas por penicilinas tienen una alta infinidad por este enzimo, y pueden inducir penicilinas si se usan en concentraciones sub-inhibitorias.

La dosificación de estas penicilinas es usualmente de 12 gramos al día en dosis divididas cada 4 horas endovenosamente. La toxicidad es idéntica a penicilina G con la adición de que la metilicina es dolorosa cuando se usa intramuscularmente y puede causar tromboflebitis cuando se usa endovenosamente. Su uso es esencialmente en el tratamiento de infecciones estafilocócicas que son resistentes a penicilina y no deben de usarse cuando el organismo es sensible a penicilina G. Como ejemplo de una penicilina semisintética resistente a penicilinas para uso oral, discutiremos cloxacilina, cuyo uso y espectro es idéntico al de metilicina pero que la dosificación por vía oral es de 500 mg cada 6 horas una hora antes de las comidas aunque puede aumentarse hasta 1 o 2 gms oral cada 4 a 6 horas si es necesario. Su absorción es efectiva y eficiente y tiene niveles séricos adecuados en 30 minutos. Su excreción, toxicidad y usos son idénticos a los de metilicina.

Hemos presentado un repaso breve de la farmacología, espectro, uso, efectos secundarios y dosificación de las penicilinas. Esperamos esto ayude a que se prescriban estos antibióticos más racionalmente.

#### REFERENCIAS

1. Adkinson, N. F., Jr., Thompson, W. L., Maddrey, W. C. and Lichtenstein, L. M.: Routine use of Penicillin skin



- testing on an inpatient service. *New Engl J Med* 285: 22, 1971.
2. Bear, D. M., Turk, M., and Petersdorf, R. G.: Ampicillin. *Med Clin North Amer* 54: 1145, 1970.
  3. Bodey, G. P. and Nance, J.: Amoxicillin in vitro and pharmacological studies. *Antimicrob Ag Chemother* 1: 358, 1972.
  4. Gilbert, D. N. and Sanford, J. P.: Methicillin critical appraisal after a decade of experience. *Med Clin North Amer* 54: 1113, 1970.
  5. Green, R. L., Lewis, J. E., Kraus, S. J., Frederickson, E. L.: Elevated plasma Procaine concentrations after administration of Procaine Penicillin G. *New Engl J Med* 291: 223, 1974.
  6. Hewitt, W. L.: The Penicillins. *JAMA* 185: 264, 1963.
  7. Johnson, W. D., Jr., Hook, E. W., Lindsey, E. and Kaye, D.: Treatment of chronic typhoid carriers with Ampicillin. *Antimicrob Ag Chemother* 3: 439, 1973.
  8. Kirby, W. M. M., Rosenfeld, L. S. and Brodie, J.: Oxacillin laboratory and clinical evaluation. *JAMA* 181: 739, 1962.
  9. Lavetter, A., Leedom, J. M., Mathies, A. W. Jr., Ivler, D. and Werhler, P. F.: Meningitis due to *histeria monocytogenes* - a review of 25 cases. *New Engl J Med* 285: 598, 1971.
  10. Lerner, P. I., Smith, H. and Weinstein, L.: Penicillin neurotoxicity. *Ann N Y Acad Sci* 145: 310, 1967.
  11. Levine, B. B. Editorial: Skin rashes with Penicillin therapy: Current management. *New Engl J Med* 286: 42, 1972.
  12. McCarthy, C. G. and Findland, M.: Absorption and excretion of four penicillins: Penicillin G, Penicillin V, Phenethicillin and Phenylmercaptamethyl Penicillin. *New Engl J Med* 263: 315, 1960.
  13. Nelson, J. D.: Antibiotic concentration in septic joint effusions. *New Engl J Med* 284: 349, 1971.
  14. Pullen, H., Wright, N. and Murdock, J. M. C.: Hypersensitivity reactions to antibacterial drugs in infectious mononucleosis. *Lancet* 2: 1176, 1967.
  15. Resnik, S. S. and Shelley, W. B.: Penicilloyl-polylysine skin test: Anaphylaxis in absence of penicillin sensitivity. *JAMA* 196: 740, 1966.
  16. Stanford, H. C., Jordan, M. C. and Kirby, W. M. M.: Clinical pharmacology of carbenicillin compared with other penicillin. *J Infect Dis (Suppl)* 122: 99, 1970.
  17. Weinstein, L., Lerner, P. I. and Chew, W. H.: Clinical and bacteriological studies of the effect of massive doses of penicillin G on infections caused by gram-negative bacilli. *New Engl J Med* 271: 525, 1964.
  18. Wise, R. L.: Modern management of severe staphylococcal disease. *Medicine* 52: 295, 1973.

## SINDROME DE HIPO-NEOGLUCOGENIA

Durante el último mes y medio he recibido en la consulta de mi oficina tres diferentes pacientes que en días diferentes cada uno, me refirieron un síndrome análogo que me interesó mucho y que sin hallar objetividad explicable pienso que pueda ser debido a un síndrome ocasionado por empobrecimiento de los músculos de su osamenta en su glucógeno muscular.

Los tres pacientes fluctuaban en su edad entre los 50 y 65 años, su piel un poco seca y el extremo externo de sus párpados en los tres muy escasos en pelos. Los tres eran de constitución magra y según dijeron, los tres habían sustituido desde hace unos meses el azúcar por sacarina y habían rigorizado la dieta con las medidas especiales de limpiar las carnes de sus alimentos carneos de la grasa que llevaban implícita, suprimido la mantequilla y substituído el azúcar sucrosa por sacarina para evitar el aumento de peso dado su corta talla.

Además, los tres pacientes refirieron que para mantener su tónica muscular practicaban la natación diariamente, sin cansarse, pero con el propósito de mantener su peso y evitar la iniciación de obesidad dada su talla moderada. Los tres pacientes eran magros, musculados, los tres tenían una matidez hepática dentro del grosor normal, estaban bien constituídos y el peñisco de la piel en el abdomen y los brazos producía un pliege aplanado. El C. B. C. estaba dentro de los límites normales en los tres y la curva de bioquímica evidenció sus metabolismos fundamentales dentro de las cifras de nor-

malidad. Uno de los tres refirió que había sufrido una crisis durante la noche, y los otros dos durante la siesta de dos a cuatro.

A los tres los despertó y alarmó unos dolores por todos los músculos especialmente de las extremidades y parte superior anterior del tórax, despertados comprobaron con sus familiares que bajo la piel los músculos, como que "temblaban" contrayéndose y descontrayéndose.

A los tres pacientes les dieron sus familiares un vaso de jugo de frutas dulcificado y ¡santo remedio! las contracciones y sus dolores cesaron.

Continuaron tomando sucrosa con el café de la mañana y el de después del almuerzo y desde entonces no han vuelto a tener ni los dolores ni el temblor de los músculos bajo la piel.

Las hormonas del Lóbulo Anterior de Hipofisis (tropicohormonas) regulan la actividad del tiroides y de la corteza adrenal que controlan en gran parte el metabolismo de los carbohidratos.

La insulina restaura el glucógeno normal en el hígado del diabético. En los individuos normales a partir del glucógeno hepático se restaura el glucógeno muscular a partir del cual se provee la glucosa que se oxida en los músculos.

Se necesita por lo tanto buena nutrición y buen aporte de carbohidratos para reponer el glucógeno muscular especialmente en los individuos que hacen ejercicio físico cotidianamente.

*Angel Rodríguez Olleros, MD*

## REFERENCIAS

1. Fisher, R. E., Pencham, R. L.: Proc. Experimental Biology Med. 34, 106, 1936.

## LA HIPERLIPEMIA EN PUERTO RICO

En este número del Boletín se publica un artículo de Cancio y León titulado "Hyperlipoproteinemic Types Among Puerto Ricans". Este viene a ser un informe final de un estudio que se llevó a cabo durante ocho años (1966-1974) en el Hospital de Veteranos de San Juan. Ya en 1966 (1) y en 1972 (2) se habían publicado informes preliminares en esta revista médica.

Se ha hablado sobre colesterol en nuestra literatura pero sobre la hiperlipemia como tal, los artículos han sido infrecuentes aunque sustanciosos. En 1970 (3) Maldonado et al informaron tres casos del raro Tipo I y repasaron detalladamente el tema. En 1971 (4) se publicó la Conferencia Magistral "Dr. Ramón M. Suárez" ofrecida por el Dr. Mario R. García-Palmieri en el año anterior. En ella él alude a los hallazgos sobre hiperlipemia que surgieron del estudio prospectivo epidemiológico de la enfermedad arteriosclerótica del corazón que él dirige. Hablando sobre el colesterol y los triglicéridos como factores de riesgo en el desarrollo de arterioesclerosis de las coronarias, el Dr. García Palmieri hizo énfasis en una rara condición, hallada con relativa frecuencia en el hombre rural joven puertorriqueño. Esta consistía en "un nivel de colesterol normal o bajo asociado con glicéridos altos". Es también de interés la observación que la incidencia de cardiopatía coronaria en estos jóvenes es significativamente menor que en la población masculina urbana de igual o mayor edad.

Detalles sobre los patrones de lipoproteínas séricas en el hombre puertorriqueño que emanaron de ese estudio fueron publicados en nuestro Boletín en 1975 (5) aparte de otros datos que se publicaron en revistas médicas estadounidenses. Es en este artículo donde se informa por primera vez la incidencia de hiperlipoproteinemias en el hombre en Puerto Rico (26.6 por ciento). Esta se obtuvo de una muestra de 1385 varones de la región noreste.

El estudio de Cancio y León en el cual clasificaron 723 casos y que motiva este editorial, conlleva también singular importancia, especialmente para el médico que ejerce en Puerto Rico, ya que señala en una población sospechosa de hiperlipemia, la incidencia de los distintos tipos (clasificación Fredrickson modificada). Además, nos da una idea más clara y segura sobre las enfermedades asociadas o no asociadas con los distintos tipos de hiperlipemia que se han descubierto en Puerto Rico. El corolario natural es que el médico puede confiar más en sus recomendaciones a los pacientes en torno a precauciones que se deben tomar y cuando, tratamientos dietéticos y/o medicinales, y pronóstico de acuerdo al tipo de hiperlipoproteinemia que demuestren.

Aunque de acuerdo con el informe de Gulbrandsen et al (5), la dieta alta en carbohidratos (CHO) no parece ocasionar marcados y/o permanentes aumentos en los lípidos séricos del sector puertorriqueño que examinaron, no creo que sea aconsejable olvidarnos de este factor. Existen casos, como el mío, en los cuales los CHO son en gran parte responsables de alzas en los lípidos y, especialmente, de la prominencia de la banda pre-beta. En éstos, una dieta baja en CHO aunque alta en grasas y proteínas puede resultar en una reducción de la hiperlipidemia. Esto se debe a que estos pacientes tienen un metabolismo de CHO defectuoso que resulta en una producción endógena, mayormente hepática, de grasas neutras. La incidencia alta de diabetes mellitus y el uso excesivo de alcohol en nuestro ambiente son factores adicionales a los cuales debe dar el médico especial atención ya que guardan una relación muy estrecha con la hiperlipemia. ¡Y no nos olvidemos de la obesidad!



Los errores que a veces cometemos en Puerto Rico en el diagnóstico y tratamiento de ciertas enfermedades se deben en parte a que no conocemos sus verdaderas incidencias y sus historias naturales como ocurren en nuestra isla. En estos casos nos vemos obligados a aplicar al pueblo puertorriqueño las experiencias, ya conocidas, pero de otros países.

Gracias a los estudios que acabamos de comentar, sabemos más de nuestra hiperlipemia. Entre otras cosas, sabemos que tiende mucho más hacia la raza Caucásica y el sexo masculino, que ocurre con mayor frecuencia en el hombre que vive en la ciudad, que los Tipos II y IV son los más comunes, que el Tipo III es prácticamente inexistente, que la incidencia de enfermedad cardiovascular es más alta en el Tipo II, que el sobrepeso y la diabetes se ven asociados frecuentemente con el Tipo IV y que deben corregirse, y que el desarrollo de xantomas tiene una incidencia baja.

Mientras se siga sospechando que los lípidos juegan un papel importante en el desarrollo de la arterioesclerosis (teoría de la infiltración) (6) tenemos que seguir de cerca el comportamiento de la hiperlipemia en Puerto Rico.

En fin, vale la pena conocer la información adicional que nos brindan Cancio y León en su último artículo. El próximo paso es llevar a cabo investigaciones similares en la población de edad escolar.

José M. Torres, MD, FACP, FACC

## REFERENCIAS

1. Cancio, M.: The Serum Lipid Picture. Bol. Asoc. Méd. P. R. 58: 563, 1966.
2. Cancio, M. and León, J. M.: Hyperlipoproteinemic Types among Puerto Ricans: a progress report. Bol. Asoc. Méd. P. R. 64: 11, 1972.
3. Maldonado, N., Frías, A. E., Cancio, M., Gulbrandsen, C. and Haddock, J.: Type I Hyperlipoproteinemia. Bol. Asoc. Méd. P. R. 62: 301, 1970.
4. García-Palmieri, M. R.: Conferencia Anual "Dr. Ramón M. Suárez". Bol. Asoc. Méd. P. R. 63: 1, 1971.
5. Gulbrandsen, C. L., García-Palmieri, M. R., Tillotson, J., Nazario, E., Costas, R. and Colón, A. A.: Serum Lipoprotein Patterns in Puerto Rican Men. Bol. Asoc. Méd. P. R. 67: 148, 1975.
6. McCullagh, K. G.: Revised Concepts of Atherogenesis. Cleveland Clinic Quarterly 43: 247, 1976.

## *SOME CHILDREN NEED ANOTHER MEASLES IMMUNIZATION*

CHICAGO — Children immunized against measles before the age of 13 months may be inadequately protected and should be reimmunized, says a research report in the Jan. 24 Journal of the American Medical Association.

Anne S. Yeager, M. D., of Stanford University School of Medicine, California, and colleagues studied the protective levels against measles in the blood of 465 children in two California counties.

Dr. Yeager found that 14.6 percent of the children immunized at 12 months of age were inadequately protected against the disease. But only 5.2 percent of those immunized at 13 months or later had inadequate protection.

The problem likely is that the younger children still had some degree of protection inherited from their mothers, and this factor interfered with the effectiveness of the vaccine, she says.

Despite a great reduction in measles with the advent of the vaccine in 1963, "the control of measles is not a solved problem," Dr. Yeager points out. Many children still have not been immunized, and some of those immunized in infancy are inadequately protected.

An accompanying editorial points out that measles in the United States had dropped from a pre-vaccine figure of half a million cases annually to some 35,000, with a corresponding drop in measles-induced encephalitis, an occasional serious affect of the disease.

The editorial says that experts in the field now recommend that measles immunization be deferred until about age 15 months for infants who live in communities where the disease is not prevalent. Vaccinations should be given any time after six months during measles outbreaks, and these children should then be re-vaccinated after 15 months.

---

## *AMA ISSUES NEW BOOK ON SKIN AND HAIR CARE*

CHICAGO — Watch out for those wild promises of creams and other cosmetics that claim to erase wrink-

les and rejuvenate aging skin. They don't do it.

Turtle oil or mink oil are no better than other oils commonly used in cosmetic preparations. No cosmetic will restore youth and beauty.

Lemon juice adds nothing helpful to shampoos or cosmetics, despite some advertising claims. Facial treatment with eggs won't actually do anything for your face.

Cosmetic products such as cold cream or face powder are basically so much alike that selection of one brand or another actually boils down to personal preference for shade, scent, texture or even package design. Price isn't necessarily a guide. Some low cost items are just as good as the more expensive offerings.

These and many other guidelines to assist the consumer in wading through the overwhelming array of claims and counter-claims of products sold to enhance personal appearance and improve skin health are offered in the new, third edition of the American Medical Association's Book of Skin and Hair Care, published this winter by J. B. Lippincott Co.

Titled *THE AMA BOOK OF SKIN AND HAIR CARE*, the third edition is an update and expansion of the earlier volume, *THE LOOK YOU LIKE*. All were edited by Linda Allen Schoen, in consultation with the MAA's Committee on Cutaneous Health and Cosmetics.

Through the years the AMA has received many thousands of queries from the public in this area. Replies were provided by physicians, Ph.D.'s, consultants in the field of cutaneous health and cosmetics, and AMA staff members. It is the answers to these questions that make up most of the material for *THE AMA BOOK OF SKIN AND HAIR CARE*.

The book includes three general areas: cosmetics, hair, and skin. Individual chapters cover topics such as cosmetic creams, rejuvenating cosmetics, reactions to cosmetics, hair dyes and bleaches, hair waving and straightening, excess hair, shaving advice, baldness, acne and blemishes, wrinkles, birthmarks, dry or oily skin, problems of hands, nails and feet, perspiration and body odor, soaps and bathing, sunlight and the skin, and esthetic surgery.

None of the presently available antiperspirants

completely stop perspiration, nor is this desirable, the book points out. Degree of perspiration control varies from 5 percent to 40 percent. To guide consumers in selecting an antiperspirant, the book includes a table listing the ingredients of more than two dozen of the most popular brands. Similar information is offered in other cosmetic areas.

The book is not available through the AMA, but may be obtained in paperback for \$4.95 from the publisher, J.B. Lippincott Co.

---

#### DEATH RATE REPORTED FOR LEGAL ABORTIONS

The Center for Disease Control, Atlanta, Ga., reported in the Jan. 31 issue of the *Journal of the American Medical Association* the death rate for legal abortion in the United States for three years, 1972-1974. Records on almost 2,000,000 legal abortions were analyzed.

Death rate averaged 3.9 for each 100,000 legal abortions, Willard Cates, Jr., M. D., and colleagues found. Death rate for continuing pregnancy and childbirth during the same three years was 14.8 per 100,000 live births.

Duration of pregnancy was the most important

risk factor. Abortions during the first 12 to 13 weeks of pregnancy carried relatively little risk. Death rates were higher for older women, nonwhites, and for those whose pregnancies were interrupted later in the cycle, Dr. Cates reports.

There were 24 deaths related to legal abortion in 1972, 26 in 1973, and 26 in 1974, the researchers found.

"Clearly, in terms of risk of death, legal abortion is a relatively safe surgical procedure when compared with such commonly performed operations as tonsillectomy or appendectomy, which have death rates of 5 per 100,000 and 352 per 100,000 respectively."

Among women older than 40 years, the death rate was more than four times that of the teenage group, which had the lowest rate. Women of non-white races obtaining legal abortions had mortality three times higher than white women.

Abortions performed at eight menstrual weeks' gestation or less carried minimal risk of death, with a ratio of 0.4 per 100,000 procedures, he says.

Abortions in the first three months of pregnancy had a death rate of 1.7 per 100,000.

#### WANTED

Family practitioner and/or internist-cardiologist by six men multi-specialty group in Mid-East Tennessee. Town of 7,000 with a drawing area of 60,000 population. Modern Clinic Building adjacent to ultra-modern 200 bed Medical Center. No investment. First year guaranteed ample salary plus multiple fringe benefits. Must be able to obtain a Tennessee Medical License and speak English fluently. Ideal situation for a U. S. or P. R. trained physician wishing to relocate in U. S. If interested, contact: Ramón Sánchez Viñas, M. D., Cumberland Clinic, 301 Hayes Street, Crossville, Tennessee, 38555, (615) 484-5171.



L I S T A D E A N U N C I A N T E S

- |                        |                 |
|------------------------|-----------------|
| 1. BELTONE ELECTRONICS | HEARING AIDS    |
| 2. BURROUGHS WELLCOME  | NEOSPORIN       |
| 3. CIBA PHARM.         | VIOFORM - HC    |
| 4. PENNWALT CORP.      | ZAROXOLYN       |
| 5. ROCHE LAB.          | LIBRIUM, VALIUM |
| 6. U. S. V. PHARM.     | HYGROTON        |
| 7. THE UPJOHN CO.      | TOLINASE        |

$\frac{20}{150}$

# H

$\frac{20}{100}$

# E A R

$\frac{20}{70}$

# I N G I S

$\frac{20}{50}$

# A S P R E C I O U S

$\frac{20}{40}$

# A S S I G H T H A V E

$\frac{20}{30}$

# Y O U H A D Y O U R H E A R I N G

$\frac{20}{20}$

# T E S T E D L A T E L Y A S I M P L Y

$\frac{20}{15}$

# C O M F O R T A B L E H E A R I N G

$\frac{20}{10}$

# I N V E S T M E N T O F A F E W M I N U T E S

Hearing losses are among the most consistently neglected health problems. Many people with them won't even admit it to themselves, let alone others. A little encouragement may start them thinking about themselves more realistically.

That's why we're offering you the poster shown here. You can hang it on the wall or stand it on a small table. It comes with booklets called "As precious as sight" that give your patients some basic facts about auditory testing and hearing losses and how easy they are to correct in many cases.

Write to us for your free poster and booklets. They just might help you to help some patients who aren't hearing as well as they used to. Even those who ordinarily wouldn't hear of it.

Professional Relations Division, Beltone Electronics Corporation  
4201 West Victoria Street, Chicago, Illinois 60646, an American company

**Beltone**  
WHEN A HEARING  
AID WILL HELP



Lidov





# ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

AUG 4 1977

BOLETIN

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE



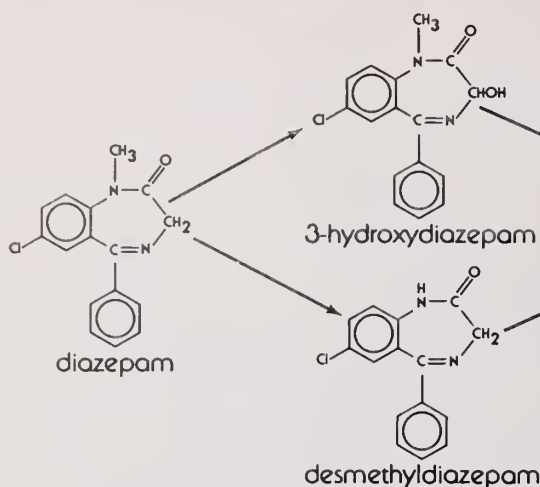
VOL. 69

Mayo

1977

No.5

# A pharmacokinetic character all its own



**Valium (diazepam) is a benzodiazepine with a distinctive pharmacokinetic profile**

The pharmacokinetic profile of Valium is one of the characteristics that sets it apart from other benzodiazepines. Consider, in particular, the metabolic pathway of Valium. The three major metabolites of Valium exhibit significant pharmacologic activity—and so, of course, does the parent substance—diazepam itself. All combine to produce the characteristic clinical response seen with Valium. The response you have come to know, to want and to trust.

Pharmacokinetic studies also demonstrate that Valium has a pattern of absorption, distribution, metabolism and elimination that is reliable and consistent. And, although the pharmacokinetics of a drug cannot, at present, be specifically related to its clinical effects, it is clearly a factor that distinguishes one product from another by providing important insights into how each moves through the patient's body.

## Valium® (diazepam) <sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:**

Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma;

may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



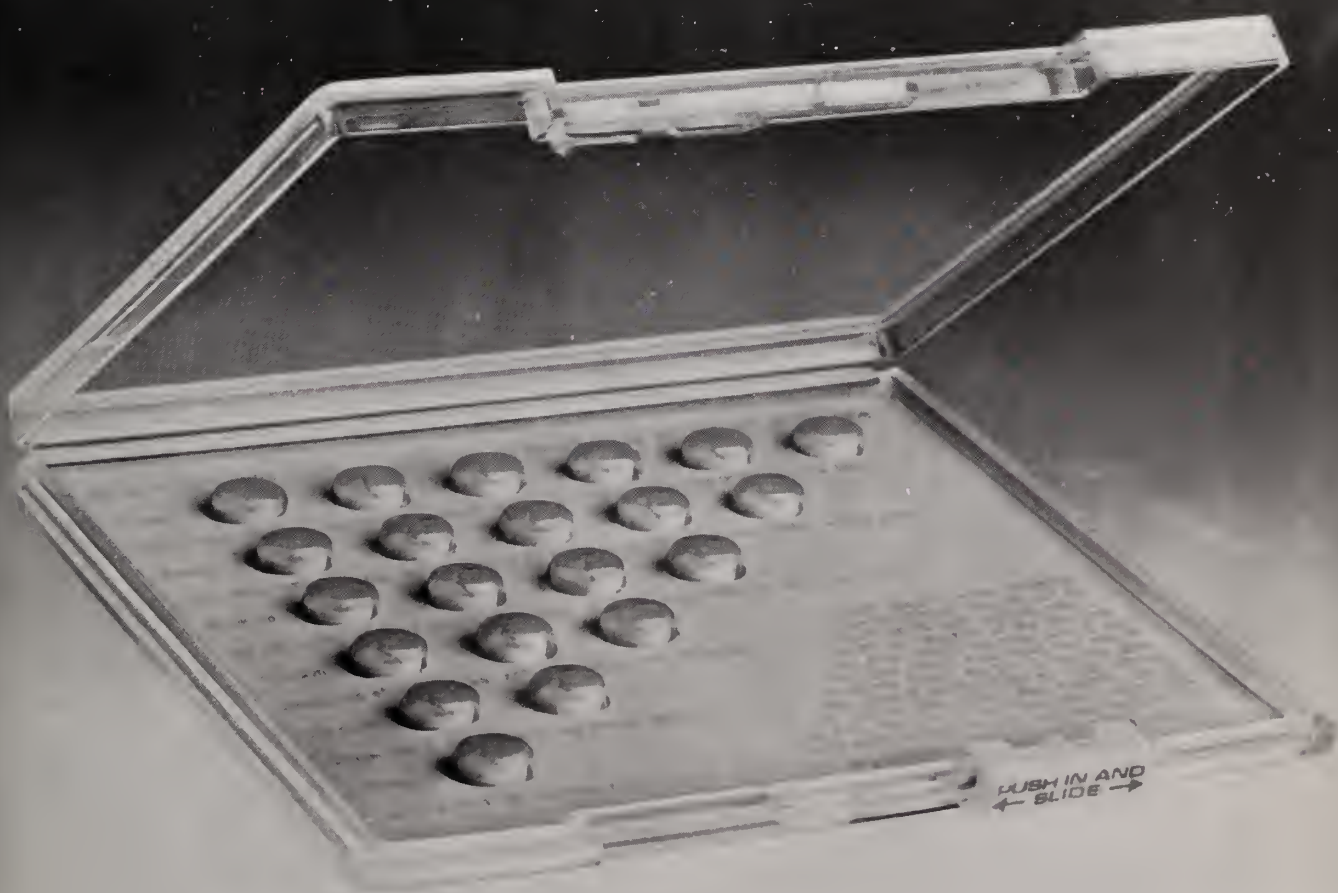
**Upjohn**

The Upjohn Company, Kalamazoo, Michigan 49001

# Medrol<sup>®</sup> 4 mg Dosepak<sup>\*</sup>

**methylprednisolone, Upjohn**

The explicit printed dosage instructions that accompany each Dosepak make it easy for the patient to understand and follow the dosage regimen.





# ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial

Fundado en 1903

Volumen 69

Mayo 1977

Número 5

## JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bernúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

## Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

## Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

## Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Health Maintenance for the Industrial Worker: A Rural Health Experience in Puerto Rico .....	145
José Ramírez Rivera, MD., FACP and Miguel H. Del Toro, MD	
Programa de las Corporaciones para los Trabajadores Incapacitados en Puerto Rico .....	152
Herman J. Flax, MD, FACP	
Successful Repair of a Right Coronary Artery — Coronary Sinus Fistula with Associated Left Coronary Arteriosclerosis .....	156
Raúl García Rinaldi, MD., L. Von Koch, MD and Jimmy F. Howell, MD	
Drug Therapy, Cardiac Pacing and Cardiac Surgery in the Wolff-Parkinson-White Syndrome. Report of Two Cases Treated with Cardiac Pacemakers .....	160
Charles D. Johnson, MD.	
Coronary Artery Disease: Natural History, Risk Factors and Management .....	167
Henry D. McIntosh, MD, and Kinsman E. Wright, MD.	
Noticias .....	176

PORTADA: Patio Interior, Fuerte San Cristóbal  
Viejo San Juan

(Cortesía — Dr. Rafael E. Ramírez)

There is only one  
*macrocrystal*  
nitrofurantoin...  
and only Eaton  
has it.

Eaton

Consistent  
potency  
against the  
most prevalent  
uropathogens.

# Macrochantin<sup>®</sup>

(nitrofurantoin macrocrystals)

capsules 25mg 50mg 100mg



**® EATON LABORATORIES**  
Norwich International  
410 Park Avenue  
New York, N.Y. 10022  
U.S.A.

**INDICATIONS:** Indicated for the treatment of pyelonephritis, pyelitis, and cystitis due to susceptible *E. coli*, enterococci, *S. aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses) and certain strains of *Klebsiella-Aerobacter*, *Proteus* and *Pseudomonas*.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function; infants under one month; pregnant patients at term; known hypersensitivity.

**WARNINGS:** May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. (Such patients should be closely observed while receiving nitrofurantoin.) Discontinue the drug at any sign of hemolysis.

Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to *Pseudomonas*. Safety not established during pregnancy and lactation; should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.

**PRECAUTIONS:** Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal

impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**ADVERSE REACTIONS—Gastrointestinal Reactions—**Anorexia, nausea, emesis are the most frequent reactions; less frequently, abdominal pain and diarrhea, rarely, hepatitis. This dose-related toxicity reaction can be minimized by reduction of dosage, especially in the female patient.

**Hypersensitivity Reactions—**Pulmonary sensitivity reactions, which can be acute, subacute, or chronic. Acute reaction is commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on X-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and resolve with cessation of the drug therapy. Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation

of the drug therapy.

**Dermatologic Reactions—**Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other Sensitivity Reactions—**Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.


**Hematologic Reactions—**Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurological Reactions—**Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

**Miscellaneous Reactions—**Transient alopecia.

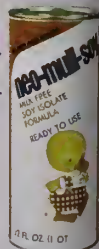
**SUPPLIED:** Macrochantin (nitrofurantoin macrocrystals) is available in opaque, yellow capsules of 100 mg (coded "Eaton 009") and in opaque, yellow and white capsules of 50 mg (coded "Eaton 008") in bottles of 30, 100, 500, and 1,000 capsules; and in opaque, white capsules of 25 mg (coded "Eaton 007") in bottles of 100 capsules. Macrochantin Capsules, 50 mg and 100 mg, are also available in hospital unit-dose packages, strip-packaged in boxes of 100.





**"Little Boy Blue,  
come blow your horn,  
The sheep's in the  
meadow, the cow's  
in the corn..."**

Since cow's milk and corn are leading causes of food allergy among infants, NEO-MULL-SOY® formula doesn't contain either one. Other leading soy formulas do contain corn syrup. Next time recommend corn-free NEO-MULL-SOY formula first. Mothers like its milky whiteness. And now it's easier for them to find NEO-MULL-SOY formula, because it's more readily available at grocery and drug stores.



**NEO-MULL-SOY®**

Soy Isolate Formula

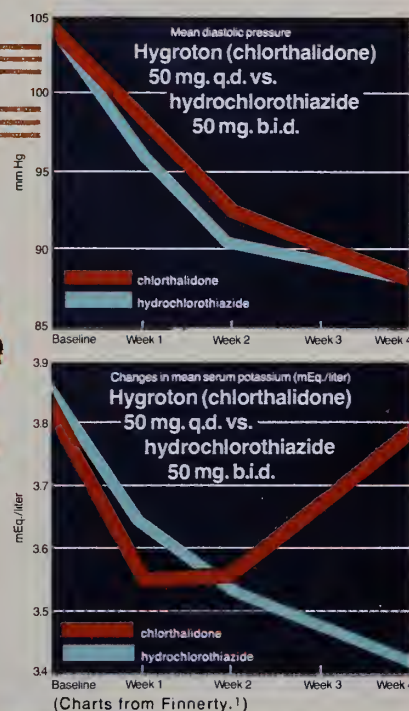
The only leading soy formula  
that's milk-free AND corn-free.

**SYNTEX**

SYNTEX LABORATORIES, INC.  
PALO ALTO, CALIFORNIA 94304



# New double-blind study In hypertension... Hygroton (chlorthalidone) vs. hydrochlorothiazide



## Hygroton achieves Goal pressure with single daily doses

"Two 50 mg tablets of hydrochlorothiazide were required to produce the same blood pressure lowering effect as one 50 mg tablet of chlorthalidone..." Frank A. Finnerty, Jr.<sup>1</sup>

## More positive potassium profile

The advantages of chlorthalidone over hydrochlorothiazide "...should be reflected in better patient compliance, because of its... potential for fewer side effects resulting from decreased potassium..."

Frank A. Finnerty, Jr.<sup>1</sup>

# Hygroton<sup>®</sup> (chlorthalidone) 50 mg. blocks sodium retention longer

### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema. **Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased,

decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. **Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn. **Usual Dose:** One tablet daily. **How Supplied:** Tablets—100 mg (white, scored) and 50 mg (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6.

**Reference:** 1. Finnerty, F. A., Jr., Hypertension: The Continuing Challenge, Scientific Exhibit, Meeting of AAFP, Boston, Mass., Sept. 20-23, 1976.

**USV  
LABORATORIES**

USV Laboratories Inc.  
Manati, P.R. 00701

# Maalox®... on balance, it's better



- **more effective**—49% more acid neutralizing capacity than the next leading antacid.\*
- **greater patient acceptance**—over 25 years' experience with millions of patients.
- **less costly**—when compared to the next leading antacid.

- **less sodium**—36% less sodium than the next leading antacid.

Minty Maalox. Well tolerated, month after month...year after year.

\*per minimum recommended dose.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034



## HEALTH MAINTENANCE FOR THE INDUSTRIAL WORKER: A RURAL HEALTH EXPERIMENT IN PUERTO RICO

José Ramírez Rivera, M.D., F.A.C.P. and Miguel H. del Toro, M.D.

**Abstract:** In the sea of the indigent, the unemployed and the unproductive, like a dwindling archipelago, languishes the Puerto Rican industrial worker. His health needs remain unsuspected; in effect they are ignored. More than 65 percent of them are willing to pay the cost of simple medical screening tests when these are offered at their place of work and without loss in pay. As many as 80 percent of the screened may have important and readily treatable clinical pathology. The study shows it is technically feasible and economically sound to bring to the factory site and the awareness of industrial workers the advantage of preventive medicine. The far-sighted health provider should engineer privileged access to health maintenance for this productive group during and after the customary government working hours. The acceptance of our plan, by workers and management suggests that health maintenance may be successful in Puerto Rico if it is tailored to the needs of the user instead of the convenience of the provider.

**Resumen-** En el mar del indigente, el desempleado y el que no produce, como un archipiélago

que se consume, languidece el trabajador de industria en Puerto Rico. Sus necesidades de salud son generalmente desconocidas; de hecho son ignoradas. Más del 65 por ciento de ellos están dispuestos a pagar el costo de exámenes sencillos de diagnóstico cuando éstos se ofrecen en su lugar de trabajo y cuando los mismos no conllevan pérdida de salario. Más del 80 por ciento de los examinados tienen patología clínica de importancia fácilmente susceptible a tratamiento.

El estudio demuestra que es técnicamente factible y económicamente viable llevar a la fábrica y a la conciencia del trabajador industrial las ventajas de la medicina preventiva. El proveedor de salud de amplia visión debe diseñar acceso privilegiado para el mantenimiento de la salud de este grupo durante y después de las acostumbradas horas laborables del gobierno. La aceptación de nuestro plan por los trabajadores y la gerencia sugiere que el mantenimiento de la salud del trabajador industrial puede tener éxito en Puerto Rico si éste se hace para cubrir las necesidades del usuario en vez de a la conveniencia del proveedor.

---

*From the Western Health Region, Office of Education and Clinical Investigation, and Rincón Rural Health Initiative Project.*

*Presented in part at the annual meeting of the 'Academia del Sur', December 3, 1976 in Ponce, Puerto Rico.*

*Request reprints to: Dr. José Ramírez Rivera, Box No. 419, Mayagüez, Puerto Rico 00708.*

Rincón is an unpretentious town in the west coast of Puerto Rico, cuddled between green hills and the turbulent waters of the Mona Passage. Eighty-five percent of its 10,000 inhabitants are medically indigent. Fishing and the





Fig. 1: Sign indicating the services offered at the Rincón Health Center.

cultivation of sugar cane, the most important occupations, do not provide a steady or predictable income. The town's economy is centered around four industries which offer jobs to 679 people when fully operational. Recently, tourism has become a growing source of income. Tourists from abroad are attracted to the nearly deserted sandy beaches, informal restaurants and overall quiet environment which contrasts with the agitated and tense metropolitan life. Tourists are discouraged, however, as are Rincón's better educated citizens, by the absence of appropriate health care.

Until 1975 health services at Rincón suffered a similar fate to that of most rural areas in Puerto Rico: There were no private physicians or dentists; the health care providers assigned by the government to the local health center had limited training and no initiative or resolve to face indigenous health problems. In July 1975 a federal grant was obtained and National Health Service Corps (NHSC) physicians were recruited to improve the ren-

dering of primary care in Rincón. In the first 18 months of operation the following goals have been attained:

1. The physician-population ratio has been reduced to 1:2500 by adding two well trained and dedicated physicians to the two provided by the Department of Health.
2. Effective treatment at the primary care level has been developed with *excellent* laboratory and X-ray services from 8:00 a.m. to 4:30 p.m. (Fig. 1) and *unfailing* emergency room coverage 24 hours a day.
3. A high quality medical practice has been ensured by the use of the problem-oriented record and by a weekly clerical and medical audit of 10 percent of the medical records of each physician (Fig. 2).
4. A two-chair dental clinic with a dentist and three dental assistants with extended functions operates until

-2-

Dr. Ramírez Rivera

December 16, 1976

Dr. Silva (cont.)

Record no. 2869 Subjective did not elaborate on urinary complaints. Objective- no rectal examination performed. Treatment- Mandelamine unnecessary. Repeat urinalysis not ordered and follow-up appointment not given.

Record no. 14464 Librax incorrectly prescribed. Diet incompletely given.

Dr. N. Figueroa:

Record no. 14938 Subjective missing, patient not identified. No problem list.

Record no. 12115 No follow-up appointment.

Record No. 14964 No follow-up appointment. Problem list incomplete.

Dr. Miguel H. Del Toro

Record No. 8881 Excellent medical record.

Record No. 792 Adequate medical record.

Record No. 13606 Adequate follow-up record.

Record no. 1459 adequate medical record.

Dr. Héctor L. Banchs:

Record no. 930 Adequate medical record.

Record no. 3247 inadequate treatment for Dysmenorrhea.

Record No. 14692 Adequate medical record.

Dr. Wilfred Hernández:

Record No. 1962 Problem not stated on problem list.

Record No. 901 Good medical record.

Record No. 13398 Good medical Record.

Fig. 2: Page from recent medical audit showing the type of audit.

5:30 p.m.

5. Health maintenance has become a proper channel for citizen participation with the development of a community governing board; there are reports of progress to the community and requests for funds from the community for specific goals.
6. The practice of medicine and dentistry has been made attractive by implementing a program of continuing education through rotations one half day

a week in the sub-specialty clinics of our Regional Hospital and ready access to consultation; another incentive has been furnishing \$600 and 5 days of educational leave a year for post-graduate courses.

7. All health care providers, whether paid by the Department of Health or the National Health Service Corps, and all funds, whatever their source, have been fused into a single operating program of comprehensive health care which is fiscally responsible.

One of our early projections was to promote adequate health maintenance among the industrial workers. For this reason, a *low-cost, prepaid* program for screening and health education was developed for three interested industries. Privileged access to health care maintenance was established by creating an afternoon clinic where workers and their families could come by appointment to be seen by a specific physician.

In this paper we present the surprising results of our initial experience with industrial health screening and maintenance.

## Methods and Subjects

Medical history questionnaires that could be answered "yes" or "no" were prepared. A separate sheet contained a printed dental chart to be used for the screening dental examination. The last sheet of the questionnaire was designed so that a copy of this sheet with the results of the laboratory tests and the physician's and dentist's comments could be mailed to the worker at his chosen address in a window envelope.

After previous arrangement with management, the screening program was announced by a physician in three factories who chose to participate. He explained to the workers the purpose and scope of the program. Participation was voluntary. A fee of \$5.00 per person was required.

Questionnaires were provided to management

TABLE I  
TEN MOST FREQUENT SYMPTOMS IN 125 WORKERS ANSWERING  
THE QUESTIONNAIRE

Symptoms	Number of Positive Answers	Percent Of Total	Examined in Clinic	Percent Attending Clinic
1. Low back pain	62	49.6	17	27
2. Frequent headaches	58	46.4	18	31
3. Difficulty sleeping, nervous	52	41.6	13	25
4. Constipation	50	40.0	11	22
5. Menstrual Problems	42	41.5 **	10	24
6. Heartburn fullness, abdominal pain after meals	42	33.6	9	21
7. Chest pain and palpitations	41	32.8	11	27
8. Frequent crying, sad most of time	38	30.4	15	39
9. Frequent upper respiratory infections ***	37	29.6	8	22
10. Problems with sexual intercourse	10	9.9	3	30

\* Some workers have multiple symptoms.

\*\* 41.5 percent were females.

\*\*\* Over twice a year.

about one week before the intended visit. Management passed them on to the interested employees for their completion and collected \$5.00 per person. The total screening fee and a list of the participating employees were then sent to the health center and a date and time was set when the "industrial health team" would visit the place of business. The team consisted of a physician, a dentist and his assistant, a laboratory technician and a practical nurse. One day before the health maintenance screening visit, plastic containers labelled with the name of each participant were sent to the factory for collection of spot urine samples. Samples were obtained within one hour of the expected arrival of the health team.

The screening was structured so as to interfere little with production. On arrival the team ran urinalyses by the Labstic method; \* meanwhile the participants lined up, five at a time, for other tests. Each brought their completed questionnaire to the practical nurse who determined their blood pressure. A blood sample

for glucose and hematocrit was obtained by the laboratory technician. The dentist and his assistant completed their examination before the subject sat next to a physician in a chair placed twenty feet from a visual acuity chart. After a rapid evaluation of visual acuity, the physician checked that all information in the questionnaire was complete. He answered specific questions about the screening exam and the industrial health clinics and assured the worker he would receive the results within ten days at his stated mailing address. After completion of the seven minute screening process the worker returned to his job.

### Results

A photocopy of the laboratory results and physician's comments was mailed to all participants within ten days of the screening exercise. Those participants with positive findings were suggested to seek the advice of their family physician or to request an appointment at the Industrial Health Clinic on Thursday afternoon from 1 pm to 5 pm. Others were suggested to have a

\* pH, glucose, protein, occult blood and acetone determination.



physical exam once a year.

The screening was not a give away; it paid for itself. The cost of screening per subject including the time of the personnel at the screening site, laboratory reagents and the thirteen-cent stamp, was \$2.65.

There were 185 employees in three participating industries producing women underwear, stuffed toys, and toilet articles. Of these, 101 females and 24 males, (67.5 percent) accepted the screening test; and 101 (80.8 percent) were found to have symptoms or laboratory findings that merited further examination.

Three months after the start of the program, 69 out of 101 (68.3 percent) workers with positive findings have attended the Industrial Health Clinic. The ten most frequent health problems identified by the questionnaire are listed in Table I.

Seventeen female sewing machine operators requested examination for low back pain. Their symptoms seemed to be related to inappropriate posture while at work.

Forty-nine workers complaining of frequent headaches also had difficulty sleeping and nervousness; 31 of them had frequent crying and sadness. Three of the 18 examined had untreated arterial hypertension. Two had chronic sinusitis, one had decreased visual acuity requiring eye glasses, five had cervical myositis, and seven had tension headaches.

Ninety-four percent of the 52 workers with difficulty sleeping and nervousness were females under age 30. Of the 13 examined, two were clearly depressed, and six were worried about finances and their spouse's unemployment. Five registered episodes of anxiety but could not pinpoint the specific cause.

Nine of 11 constipated patients refused to use the factory's bathroom facilities for two reasons: They were not allowed to use them except on coffee breaks, when there was a long waiting line, or they considered the bathroom facilities unclean.

Seven of 10 workers examined for menstrual problems, had pelvic pains during the first two days of menstruation. Five had irre-

gular menstrual period, and five perceived their menses as irregular because of insufficient knowledge of the normal variations of the menstrual cycle. On pelvic examination 2 had chronic cervicitis but none had positive Papanicolaou smears.

The nine patients with heartburn who came to the clinic had gall bladder and upper gastrointestinal x-ray studies. One had a deformed duodenal bulb, two had esophageal hiatal hernias and two had no contraction of the gall bladder after fatty stimulation. No organic disease was found in the other four.

Eleven females examined that answered "yes" to chest pain and palpitations, also complained of difficulty sleeping, frequent crying, and being sad most of the time. *None had heart disease.* One had a diffusely enlarged thyroid, but the serum concentrations of L-triiodothyronine (T3) and L-thyroxine (T4), and the radioactive iodine uptake were within normal limits.

The 15 females examined who registered frequent crying in the questionnaire also manifested other signs and symptoms of depression. Twelve (80 percent), expressed serious problems with unemployed husbands who drank heavily; nine of the 15 mentioned that their husbands had mistresses.

Twenty-eight of the workers who complained of frequent respiratory infections, worked in a stuffed-toys factory. Two of the eight seen in clinic showed chronic sinusitis, but six had no respiratory complaints at the time of the clinic visit. An evaluation of the environmental conditions in the factory is under consideration.

Ten female workers, ages 22 to 32, had problems with sexual intercourse. All admitted to frequent crying and being sad most of the time. Nine of them also had frequent headaches. The 3 who came for examination were depressed. Their husbands had mistresses in all 3 cases.

The health problems identified by the simple screening tests used are presented in Table II.

TABLE II  
HEALTH PROBLEMS IDENTIFIED BY THE SIMPLE SCREENING

Observations	Number of Cases Identified	Percent of Total	Examined in Clinic	Percent that Attended Clinic
1. Dental Problems requiring dental care	80	64.0	*	*
2. Low Hematocrit	24	19.2 **	9	38
3. Decreased visual acuity	14	11.2	1	7
4. Microhematuria	5	4	5	100
5. Elevated blood pressure	5	—	5	100
6. Elevated blood glucose	1	0.8	1	100

\* Dental facilities were not available yet when study was completed.

\*\* All females.

Sixty-four percent of the workers examined had periodontitis. One half of these had lost 6 or more teeth because of inadequate oral hygiene.

Twenty four females had a hematocrit below 38 percent. The nine examined had iron-deficiency anemia. The 15 who failed to come to our clinic were mailed prescriptions for ferrous sulphate three months after their screening examination. It was suggested that if they had not done so already, they seek medical attention 3 weeks after completing 30 days of treatment to recheck their hematocrit.

The seven workers with decreased visual acuity had never worn glasses. Only four of them were subjectively aware of their impairment.

Three of five workers with microhematuria were females menstruating at the time of the screening, and subsequent urinalyses were normal. One was a young man with prostatitis, and the hematuria disappeared with treatment. The other was a female with acute cystitis which was easily treated.

Five new cases of arterial hypertension were discovered and confirmed. The highest diastolic pressure observed was 110. Four of these were over age 40 and one was age 33.

At this writing, they have kept their clinic appointments and they are normotensive with treatment.

The one new case of adult-onset diabetes diagnosed has been easily controlled on oral hypoglycemics.

A man aged 59 mentioned difficulty voiding in the questionnaire. An enlarged prostate and elevated BUN was found on examination. The obstruction was treated successfully with a transurethral resection.

A 57 year old worker, a known adult-onset diabetic, was found to have a nodule in the left lobe of the prostate, which proved on biopsy to be a carcinoma in situ. Radiotherapy treatment were promptly instituted.

### Comments

The industrial workers in Rincón do not have an appropriate plan for their health maintenance. As many other middle and low income families, their search for primary health care is difficult and sometimes fruitless. Before we initiated our program the only inexpensive source of potentially good primary care was the Regional Hospital. The worker had to choose between losing a day's pay - competing with the indigent and unemployed in long waiting

lines at the Regional Hospital - or pay for their medical attention at the private sector. Most of the workers have families of six or more members and an income that varies between \$315 and \$412 a month. Their jobs are not permanent and they are unemployed two to three months a year. Having to pay medical bills at the customary physicians' rates is a financial burden for some and an impossibility for others. The worker who must depend for his primary care at the Regional Hospital frequently has to wait two or three months for a clinic appointment, and sometimes only to be seen for a few minutes by a harassed, recently graduated intern.

In developing a privileged access to health care for industrial workers and their families, we considered the following factors:

1. Health care should be near at hand.
2. Services should be as comprehensive as can be offered on an ambulatory basis.
3. Services should be efficient and timed so as not to interfere with gainful employment.
4. The cost of medical care should vary with the patient's income if not paid by insurance.
5. The quality of care must meet or exceed medical standards in the private sector.
6. The health care offered must provide adequate patient satisfaction.

To successfully accomplish our plans we are giving some attention to an extremely important aspect of health care about which there is much discussion but little action: Proper health education is needed to prevent disease and its complications. Health maintenance reduces hospitalizations and lowers treatment costs; in a working society health maintenance

increases productivity and lowers absenteeism.

Our observations have provided us with objective data to help direct the development of appropriate primary care in Rincón. As a result we have obtained the services of a Psychology consultant to help us define the management of our many emotionally troubled patients. A radiology consultant reads all our intravenous pyelograms, barium enemas and upper gastrointestinal studies once weekly. He also reviews all our questionable films. We also count with the services of an ophthalmologist who sees without delay from five to seven referrals once a week for a fee of \$50.

We are seeking help to develop a medical prepaid plan for two industries that lack medical insurance. Their managers are enthusiastic about the idea. Such a plan would create a steady source of income for the Health Center while providing better primary care at lower cost to the workers.

### Conclusions

The Commonwealth will be better served if we engineer privileged access to health maintenance in dental and health clinics during and after usual government working hours for one productive segment of our society — the industrial worker.

It behooves all of us who are designing plans for primary health care, *and it is economically sound*, to bring to the factory site and awareness of the industrial worker the wisdom of preventive medicine.

The information and results obtained; and the acceptance of the program by management, the workers, and the community indicate that a properly designed health maintenance program for the industrial worker may be successful in Puerto Rico.



## PROGRAMA DE LAS CORPORACIONES PARA LOS TRABAJADORES INCAPACITADOS EN PUERTO RICO

Herman J. Flax, M.D., F.A.C.P.

Cincuenta años atrás el Doctor Peabody pronunció una frase muy acertada que define perfectamente la filosofía del fisiatra. Dijo así: "El secreto de cuidar adecuadamente al paciente estriba en ocuparse de él." (1).

Hace dos años el doctor Walter Menninger escribió: "La vida es un constante proceso de adaptación entre el individuo y el ambiente en que vive". (2)

Un pensador actual y columnista de periódico, Max Lerner, citó recientemente a Abraham Lincoln, el gran realista, posiblemente el pensador más profundo que jamás ha ocupado la Casa Blanca de los Estados Unidos de América, quien dijo: "Si bien al principio únicamente podemos conocer donde estamos y hacia dónde nos dirigimos, sí podemos, sin embargo, ser buenos jueces de lo que hacemos y así hacerlo mejor". (3)

Lerner decía que vivimos en una era de negación de sueños; hablaba del realismo actual del ciudadano común, que sueña con la búsqueda de la felicidad y la consigue inmediatamente, sueña con la fama y la consigue en un abrir y cerrar de ojos, sueña con la salud y aparece ésta como por arte de magia, sueña con un cuerpo bello y lo consigue enseguida . . . Por supuesto, su disertación no se refería a las personas incapacitadas, sino al modo normal de

vida de los Estados Unidos y en especial la política. Pero también los incapacitados tienen esos sueños, y hasta es posible que ellos sean el grupo de personas más afectado por la negación de sueños.

A pesar de que los programas de medicina física y rehabilitación para los incapacitados han sido cuidadosa y extensivamente documentados, hay aún un enorme lago por parte de la comunidad y de manera especial de la industria, que no acepta a tales personas en su sistema de trabajo. Todos nosotros conocemos personas que han superado su incapacidad y han dejado su huella dentro del moderno y competitivo mundo del trabajo. Hemos oído hablar también de pequeñas industrias manejadas exclusivamente por incapacitados, pero no son muchas. Hay numerosos talleres de ambiente protegido que se dedican a fabricar principalmente piezas, y algunos, como los afiliados al programa de terapia incentiva (o industrial) de los hospitales de la Administración de Veteranos, que producen una variedad de productos. Pero la mayoría de ellos son empresas manufactureras secundarias, subcontratadas, en las que gran parte de los gastos son costeados por organizaciones filantrópicas o agencias estatales o federales. A lo largo de los Estados Unidos de América y de Puerto Rico, la tarea de preparar a los ciudadanos incapacitados para un empleo es responsabilidad del consejero vocacional o del oficial de entrenamiento vocacional, quienes preparan a estas personas y luego tratan de que las industrias se interesen en aceptarlos. Nadie negará que este es un buen procedimiento. De

---

*Del Servicio de Medicina de Rehabilitación del Hospital de la Administración de Veteranos, San Juan, P. R., y la Escuela de Medicina de la Universidad de Puerto Rico, P. O. Box 4867, San Juan, Puerto Rico, 00936.*

hecho, las estadísticas anuales prueban lo fructífero de este método.

Recientemente, en los Estados Unidos de América, este programa ha recibido un estímulo por parte de la sección 503 del Acta de Rehabilitación del año 1973 (P.L. 93-112, Sect. 503), que hace que cada negocio o compañía que ascienda a los \$2,500 en contratos de gobierno estén obligados a tener un programa de acción afirmativa para emplear al incapacitado.

Rehabilitación Internacional de los Estados Unidos de América (RIUSA) inició en esta misma fecha el llamado "Proyecto Puertorriqueño," Subvencionado por la compañía F. W. Woolworth, se llevó a cabo un estudio sobre las necesidades de los incapacitados en Puerto Rico, y se hicieron pruebas del potencial y recursos existentes para propósitos de rehabilitación.

El 15 de noviembre de 1973, RIUSA llevó a cabo una reunión en Puerto Rico con fines de planificar. Se formó un comité orientador en Puerto Rico compuesto de prominentes profesionales, voluntarios, y eminentes industriales interesados en rehabilitación.

El 8 de febrero de 1974, el proyecto había desarrollado en Puerto Rico tres objetivos:

- 1) Estimular más actividad voluntaria,
- 2) Identificar los programas federales e insulares de rehabilitación vocacional, y
- 3) Desarrollar un sistema de talleres de ambiente protegido.

Las actividades voluntarias pueden estimularse mediante esos ciudadanos conscientes de la necesidad de que la parte privada se envuelva en el desarrollo de programas de servicio social para ayudar al incapacitado. Miembros del consejo de RIUSA, muchos de ellos voluntarios decididos, pueden ser de gran ayuda para estas personas incapacitadas. Es necesario también solicitar ayuda a corporaciones nacionales e internacionales que no toman generalmente mucha parte activa en programas de asistencia pública en Puerto Rico. RIUSA tiene establecidos contac-

tos con las mayores fuentes de ayuda no relacionadas con el gobierno.

Desde el principio resultó obvio que lo primero que debía hacerse antes de desarrollar el programa era identificar claramente los programas federales existentes en todas sus categorías. Hay una cierta confusión entre departamentos que no saben exactamente lo que hacen los otros departamentos. Aún dentro de los mismos departamentos hay confusión debido al capricho y la excentricidad de la legislación federal sobre fondos públicos. Hay una serie de programas funcionando en los Estados Unidos de América que por varias razones no están activos en Puerto Rico, pero podrían estarlo, puesto que hay fondos disponibles. Estos programas deben ser identificados, debe descubrirse la razón por la que no se asignan fondos para ellos, y deben darse los consiguientes pasos a fin de que dichos fondos sean asignados. Por último, deben identificarse específicamente los programas del Estado Libre Asociado para evitar los duplicados y para tratar de conseguir mayor apoyo insular.

En Puerto Rico hay gran necesidad de talleres de ambiente protegido, más talleres como aquellos que hay para ciegos y que están respaldados y dirigidos por el Gobierno Insular, pero no hay fondos asignados para ellos. Estos talleres son el mejor modo de satisfacer realmente las necesidades de los diferentes sectores de la comunidad puertorriqueña de rehabilitación, como un esfuerzo conjunto. En ellos deberían estar envueltos el Departamento de Trabajo de los E.U.A. en las áreas de empleo y regulaciones, y el Departamento de Fomento Económico de Puerto Rico en las áreas de economía y creación de empleos. Los talleres de ambiente protegido son una faceta tradicional dentro de la rehabilitación vocacional, y hasta el Departamento de Educación necesita de ellos, ya que, por ley, este departamento no puede continuar prestando servicios a los retardados una vez hayan cumplido los 21 años de edad. Sería una magnífica solución para estos muchachos adultos la creación de estos

tipos de talleres de trabajo.

Si el proyecto llegara a construir estos talleres, Fomento estaría en posición de ofrecer asistencia técnica en cuanto a personal, orientación y la supervisión de personal experto. En este momento Fomento no puede prometer ninguna fábrica a pesar de que en ocasiones éste proporciona edificios para la industria nueva. Bajo la actual legislación, la Administración de Pequeñas Industrias está autorizada a ayudar a agencias con fines no pecunarios en la construcción de talleres de ambiente protegido. Se llegó a la conclusión de que supone una gran ventaja promover talleres "primarios" (los que producen artículos, en su mayor parte para el turismo) en vez de promover talleres "secundarios" (los que producen artículos, en

su mayor parte para el turismo) en vez de promover talleres "secundarios" los que fabrican artículos para las demás industrias según las necesidades actuales y bajo contratos individuales. Ambos son trabajos productivos, pero los talleres primarios tienen la ventaja de crear industrias y reducir la importación de las mercaderías.

Y así, el 28 de marzo de 1975, después de casi dos años de investigación de las necesidades de los incapacitados en Puerto Rico, el señor Ellis Reida de RIUSA presentó al comité puertorriqueño de orientación una propuesta para explorar el rol corporativo en la rehabilitación del incapacitado en Puerto Rico y para establecer un programa activo para conocer las necesidades de ese rol. La primera fase del proyecto puertorriqueño recibió ayuda económica de varias corporaciones privadas de los E. U. A.

Se llevó a cabo un Seminario de Planificación auspiciado por las Corporaciones para asistir a la gente incapacitada puertorriqueña los días 26 y 27 de junio de 1975 en Dorado, Puerto Rico. El propósito primordial de esta actividad fue enseñar a las corporaciones a cómo utilizar al incapacitado más sistemática y eficazmente. Las personas más preparadas en cuanto a salud y rehabilitación de Puerto Rico explicaron la situación local y ayudaron a

encauzar las deliberaciones. Fueron invitados, además, expertos distinguidos en rehabilitación de los E. U. A. para escuchar y participar activamente en las discusiones.

El Seminario resultó único en Puerto Rico por la grandísima participación de la industria privada además de los trabajadores públicos en el campo de la rehabilitación. Se trataron dos tópicos:

- 1) El impacto que tendría sobre la industria el requisito de una acción afirmativa, y
- 2) Las necesidades vocacionales de los incapacitados en Puerto Rico.

Los panelistas discutieron después sobre cuatro temas, que a su vez fueron estudiados más tarde en grupos separados. Dichos temas fueron:

- 1) La legislación de acción afirmativa,
- 2) La rehabilitación del alcohólico en la industria,
- 3) La rehabilitación del drogadicto, y
- 4) Las necesidades de los niños incapacitados.

Al finalizar el día hubo una sesión general en la que fueron presentados los programas modelo sugeridos. Y para finalizar, hubo "La Respuesta Colectiva a los Programas Modelo Presentados," un informe hecho por los industriales acerca de su punto de vista respecto a una participación conjunta, apropiada y activa.

Este seminario fue patrocinado por siete de las mayores industrias de Puerto Rico: La Commonwealth Oil Refining Co., La Continental Can Co., la International Business Machines Corp., la General Electric Co., la Procter and Gamble Co., F. W. Woolworth Co. y Xerox Corp. Fue una reunión sincera y envolvía definitivamente a las corporaciones en el rol activo de producir un programa permanente para ayudar al incapacitado en Puerto Rico.

También se propuso la creación de un comité oficial Puertorriqueño consultivo o directivo con personal debidamente seleccionado. Esto se llevó a cabo el 13 de agosto de 1975. El presidente elegido fue Mr. Derek Rodgers de F. W. Woolworth Corp.: Vicepresidente, Dr.



Herman J. Flax, de la Administración de Veteranos; tesorero, Mr. Luis Serrano Vega, Director de los Programas de Rehabilitación Vocacional del Departamento de Servicios Sociales; y secretaria, Miss Anita Costas, de Xerox Corp. Se propuso un presupuesto de \$60,000 y se instituyeron unas reuniones bimestrales. El primer plan que se presentó fue para combatir "El alcoholismo y la drogadicción en la comunidad puertorriqueña."

Para esta fecha, RIUSA recibió una donación de \$250,000 del Departamento de Comercio de E. U. A. para hacer un estudio y preparar un programa a lograr que los incapacitados en desventaja pudieran ser admitidos o readmitidos en los empleos en las industrias privadas en Puerto Rico. Este donativo titulado "Programa de las Corporaciones para los Trabajadores Incapacitados en Puerto Rico," fue fundada comenzando el 1 de enero de 1976. Pueden encontrar una relación detallada de esto en el Boletín Informativo Núm. 22 de Rehabilitación Internacional USA., 20 W. 40th St., New York, N. Y. 10018.

El entusiasmo que reina en este programa es contagioso. Mientras que en la reunión de diciembre de 1975 se atendieron a 28 miembros, en febrero de 1976 estuvieron presentes 53. A las cuatro semanas de operación, los miembros pertenecientes al programa en Puerto Rico o habían sido ya contratados o estaban siendo activamente solicitados. Se llevaron a cabo inmediatamente planes para el desarrollo del sistema, para identificar y establecer categorías con precisión, tanto de los trabajos con que se contaba como del personal incapacitado que estaba preparado o tenía la capacidad para realizarlos. RIUSA donó en abril de 1976 el costo del tiempo de una computadora para facilitar la eficiente selección de trabajos que cuadraban con los fines del programa. Para esta fecha estaban envueltos activamente en el proyecto la Alianza Nacional de Comerciantes con 100 miembros, la Cámara de Comercio de Puerto Rico con 2,500 miembros y la Asociación de Manufactureros con 500 miembros.

El propósito que ha impulsado a este programa desde sus mismos comienzos por parte

de la comunidad de las corporaciones en Puerto Rico ha sido sumamente sincero. Las corporaciones más importantes y multinacionales de los Estados Unidos, de las cuales hay 512 con representación en Puerto Rico, han sacado adelante con completo éxito la primera fase del proyecto, organizar un programa preciso para devolver de nuevo a las personas incapacitadas al mundo del trabajo y la producción. Y la representación que RIUSA tiene en Puerto Rico para este menester, "El Comité Orientador Puertorriqueño," ha cumplido a la perfección con la meta que RIUSA le fijó: "ofrecer los recursos de la Comunidad en E. U. A. para todos los lesionados del mundo." En cuanto a Puerto Rico, este ha sido el primer esfuerzo exitoso en conseguir que la industria de entrenamiento y empleo a los ciudadanos incapacitados. En ningún momento hay o habrá disminución de las fuentes de trabajo del gobierno Federal o Estatal, ambos operando en Puerto Rico. Al contrario, siempre ha habido y seguirá habiendo un estrecho contacto entre todos los grupos y agencias.

La década del '70 ha sido proclamada como la "Década de la Rehabilitación" por Rehabilitación Internacional, un programa global surgido para movilizar las fuentes internacionales de servicio al incapacitado. El Programa de las Corporaciones para Emplear a los Trabajadores Incapacitados en Puerto Rico es un ejemplo excelente de rehabilitación vocacional en acción, la meta final más deseada, el empleo del trabajador incapacitado. Puerto Rico, con todas sus fuentes en la industria, gobierno y personal, es, realmente, un magnífico campo de prueba para este proyecto. Y en consecuencia, la experiencia conseguida en Puerto Rico puede servir de gran ayuda para las organizaciones y corporaciones no solo vecinos del Caribe, sino de todo el mundo.

## REFERENCIAS

1. Peabody, W.: "The Care of the Patient", J.A.M.A., 88: 877-882, 1927.
2. Menninger, W. W.: "Caring" as part of health care quality. J.A.M.A., 234: 836-837, 1975.
3. Lerner, M.: "Mensajes, Mensajes." El Mundo, San Juan, P. R., p. 6-A, enero 31, 1976.

## SUCCESSFUL REPAIR OF A RIGHT CORONARY ARTERY — CORONARY SINUS FISTULA WITH ASSOCIATED LEFT CORONARY ARTERIOSCLEROSIS

Raúl García-Rinaldi, M.D., L.Von Koch, M.D., and Jimmy F. Howell, M.D.

**Abstract:** A 67-year old woman underwent successful repair of a right coronary artery - sinus fistula as well as aortocoronary bypass for stenosis of the left anterior descending coronary artery. The patient had experienced fatigue, exertional dyspnea, nocturnal angina and a continuous heart murmur. She represents the seventh reported successful correction of a right coronary artery - coronary sinus fistula, and the first with simultaneous coronary artery bypass for coronary arteriosclerosis.

The popularization of selective coronary arteriography has increased the discovery of coronary artery - cardiac chamber fistulas. However, these cardiac anomalies are still uncommon and the ones successfully treated even rarer.

Krause (4) described the first case of a coronary artery fistula (CAF) in 1865. Bjork and Crafoord (1) reported the first successfully corrected coronary artery fistula in 1947. Since then, only 171 coronary artery fistulas have been successfully treated surgically and reported. Rarer still are coronary artery - coro-

nary sinus fistulae. Rittenhouse (7) in his review found 13 cases of which only six involved the right coronary artery (RCA). None of the previously reported cases required an aortocoronary bypass at the time of repair of the coronary artery fistula. We now describe a patient who underwent successful correction of this rare combination of lesions.

### Case Report

A 67-year old white female presented to The Methodist Hospital for evaluation of fatigue, dyspnea on exertion, palpitations, and substernal discomfort all of recent onset. She had a previously discovered heart murmur, but had led a normal life.

Physical examination revealed a well-developed woman in no distress. The blood pressure was 155/65 mm Hg. She had a regular pulse with rate of 84/min. Examination of the heart revealed a left ventricular lift and a continuous murmur loudest in diastole over the base of the heart. There was no clinical evidence of heart failure.

Electrocardiogram (EKG) revealed left ventricular hypertrophy with strain. Chest roentgenogram disclosed cardiomegaly and prominence of the pulmonary vessels. An echocardiogram revealed normal heart valves.

At right and left heart catheterization, the atrial and ventricular pressures were normal. Oxygen saturations demonstrated a step-up at the low right atrial level. Cardiac output was 7.0 L/min with cardiac index 5.1 L/min/m<sup>2</sup> (2) by the dye dilution technique. Selective right coronary arteriography demonstrated a dilated tortuous right coronary artery with fistulous drainage

---

*From the Cora & Webb Mading Department of Surgery, Baylor College of Medicine, Houston, Texas.*

*Address reprint requests to: Raúl García-Rinaldi, M. D., Cora & Webb Mading Department of Surgery, Baylor College of Medicine, 1200 Moursund Avenue, Houston, Texas 77030.*



Figure 1

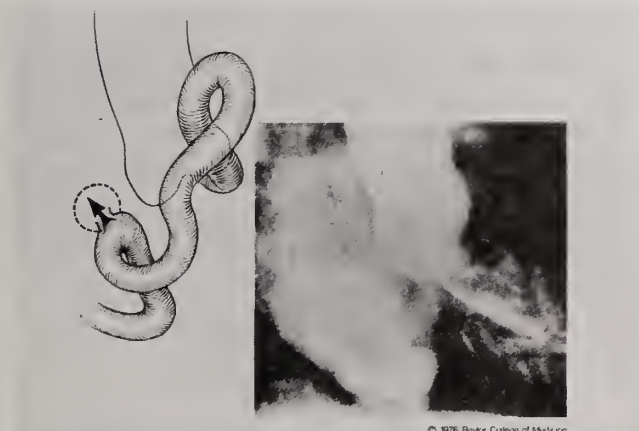


Figure 2

into the right atrium (Figures 1, 2). A left coronary arteriogram revealed an 80 percent stenosis of the left anterior descending (LAD) coronary artery.

Surgical correction was performed through a median sternotomy (Figure 3). The heart appeared slightly enlarged with a prominent, dilated, serpentine right coronary artery. A thrill was palpable over the coronary sinus. An atherosclerotic plaque was palpable in the LAD coronary artery.

Utilizing total cardiopulmonary bypass and ischemic arrest, a saphenous vein bypass from the ascending aorta to the distal LAD coronary artery was performed. After cardiac action was restored, cardiopulmo-

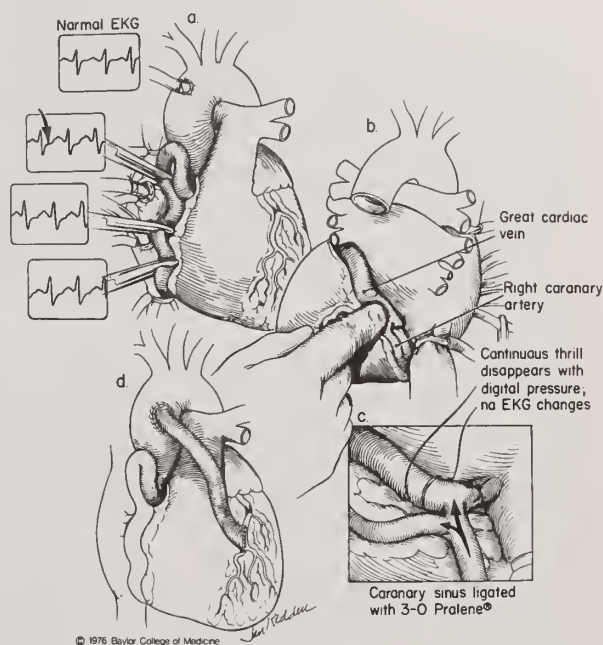


Figure 3

nary bypass was discontinued, although the atrial and aortic cannulae remained in place.

Utilizing electrocardiographic (EKG) monitoring, the right coronary artery was temporarily occluded at several points along its course to the communication with the coronary sinus (Figure 3). Occlusion at each of these levels produced ST segment changes in the EKG and hypotension. Temporary occlusion of the coronary sinus with a finger at the site of the fistula eliminated the thrill, without producing EKG or blood pressure changes. Total cardiopulmonary bypass was re-instituted. The coronary sinus was ligated at a point proximal and distal to the fistula with 3-0 Prolene®. The cardiac rhythm and configuration of the EKG remained stable. Upon cessation of cardiopulmonary bypass the patient sustained an adequate cardiac output and no electrocardiographic changes were noted.

Postoperatively, the patient's course was uneventful. No murmur could be detected. Serial EKG's were unchanged. The patient was discharged on no medications and after one year continues completely asymptomatic.



## Comments

Haller and Little (2) reported the first successfully corrected coronary artery fistula to the coronary sinus in 1963. Since then very few patients have been treated surgically. Rittenhouse (7) found only 13 coronary artery fistulae to the coronary sinus (including 6 from the right coronary artery) which had been treated surgically.

Most coronary artery fistulae involve the right coronary artery and the right atrium or right ventricle are more frequently symptomatic than fistulae into other cardiac chambers (6). The reason for this phenomenon is not known (6).

The patient we describe experienced fatigue, dyspnea on exertion, palpitations, and angina, symptoms frequently described in patients with coronary artery fistulae. She also had a continuous murmur at the base of the heart. Haller and Little (2) described the diagnostic triad for coronary artery fistulae: (1) an abnormal localization for a to-and-fro murmur; (2) a left to right shunt at the atrial or ventricular level; and (3) a large, tortuous coronary artery seen at coronary angiography. Thus, our patient presented all the clinical and diagnostic features of this condition.

The atherosclerotic stenosis of the LAD coronary artery rendered this patient unique. Rittenhouse et al. had suggested that coronary artery fistulae could cause premature coronary arteriosclerosis (7). In this patient we were unable to determine the exact causal relationship between the right coronary artery — coronary sinus fistula and the obstruction in the left anterior descending artery. Likewise, from the data obtained, we were unable to determine which of the two anatomic defects was the cause of the patient's angina.

In asymptomatic patients with coronary artery fistulae, correction should be performed to prevent complications. These patients may develop subacute bacterial endocarditis, congestive heart failure, formation and rupture of coronary artery aneurysms, obstruction of adja-

cent structures by the fistula, and myocardial ischemia or infarction. Symptomatic patients such as ours, possess definite indications for surgical treatment.

Our patient was corrected through a median sternotomy since most coronary artery fistulae can be approached with this incision, and because she required an aorto-coronary bypass. We utilized cardiopulmonary bypass for the saphenous vein bypass and for safe manipulation of the heart during exploration of the fistula. We utilized the procedure previously recommended by others: temporary occlusion of the fistula, or proximal segment of coronary artery, with simultaneous EKG monitoring. Our patient exhibited marked posterior left ventricular ischemia manifested by ST segment changes and hypotension. The surgeon must therefore carefully select the site of repair, so as to deplete the fistulous chamber of all coronary steal, while depriving the coronary bed of as little arterial flow as possible. Ligation of the coronary sinus was necessary in our patient to close the fistula without producing myocardial ischemia.

## Summary

A 67-year old female with a right coronary artery — coronary sinus fistula and left anterior descending coronary artery stenosis is reported. Preoperatively she had fatigue, dyspnea on exertion, palpitations, nocturnal angina, and a continuous murmur. The patient was treated by ligation of the fistulous communication and an aortocoronary bypass using cardiopulmonary bypass. She had no complications and was relieved of her symptoms.

## References

1. Bjork, G., and Crafoord, C.: Arteriovenous Aneurysm on the Pulmonary Artery Simulating Patent Ductus Arteriosus Botalli, *Thorax* 2: 65, 1947.
2. Haller, J.A., Jr., and Little, J. A.: Diagnosis and Surgical Correction of Congenital Coronary Artery — Coronary Sinus

Fistula, *Circulation* 27: 939, 1963.

3. Halpert, B.: Arteriovenous Communication Between the Right Coronary Artery and the Coronary Sinus, *Heart* 15: 129, 1930.
4. Krcuse, W.: Über den Ursprung Einer Akzessorischen a. Coronaria Aus Der a. Pulmonalis, *z. Ratl. Med.* 24: 225, 1865.
5. McNamara, J. J., and Gross, R. E.: Congenital Coronary Artery Fistulas, *Surgery* 65: 59, 1969.
6. Ogden, J. A., and Stansel, H. C.: Coronary Arterial Fistulas Terminating in the Coronary Venous System, *J. THORAC. CARDIOVASC. SURG.* 63: 172, 1972.
7. Rittenhouse, E. A., Doty, D. B., and Ehrenheft, J. L.: Congenital Coronary Artery - Cardiac Chamber Fistula, *Ann. Thorac. Surg.* 20: 468, 1975.

Sabbagh, A. H., Schocket, L. I., Griffen, T., Anderson, R. M., Goldberg, S., Fritz, J. M., and O'Hare, J.: Congenital Coronary Artery Fistula, *J. THORAC. CARDIOVASC. SURG.* 66: 794, 1973.

# DRUG THERAPY, CARDIAC PACING AND CARDIAC SURGERY IN THE WOLFF-PARKINSON-WHITE SYNDROME

## Report of Two Cases Treated with Cardiac Pacemakers

Charles D. Johnson, M. D.

**Abstract:** Two patients with the WPW syndrome are reported in whom permanent cardiac pacemakers were implanted for control of tachyarrhythmias. Drug therapy, cardiac pacing and cardiac surgery in the management of arrhythmias in these patients are reviewed.

**Resumen:** Se presentan en esta comunicación dos pacientes con el síndrome de Wolff-Parkinson-White, en los cuales se logró el control de episodios de taquiarritmias mediante la implantación de marcapasos permanentes. También se hace una discusión de la terapia farmacológica, con marcapasos y cirugía en pacientes con este síndrome.

The Wolff-Parkinson-White (WPW) or pre-excitation pattern has an incidence of 0.1-3.1 per 1000 population. Cardiac arrhythmias complicate the course of these subjects in 30-80 percent of cases; however, the majority are relatively asymptomatic, and indeed, are unaware that they possess the electrocardiographic abnormality. No therapy of these individuals is required, and their life may be normal except for the occasional unfortunate who is misdiagnosed as having had a myocardial infarction. This fascinating entity was recognized in 1930,

but has received increasing interest in recent years (1-4).

In a large portion of cases requiring therapy, single or combination drug therapy, cardioversion or vagal maneuvers suffice to control their arrhythmias (1, 3-9). Unfortunately, there exists a very small group of patients with frequent, recurrent and persistent tachyarrhythmias in whom all modes of presently available medical means fail to prevent or terminate their intractable arrhythmias. In this latter group, pacemaker therapy, sometimes in conjoint use with antiarrhythmic medications, or a surgical approach may be indicated. I wish to report two such patients in whom pacemaker implantations were performed, from a large group of WPW patients seen here.

### Case Reports

#### Case 1:

This is a 51-year-old female with a history of palpitations for many years, apparently refractory to antiarrhythmic drugs. In 1973, a demand coronary sinus pacemaker was placed, for termination and suppression of attacks of tachycardia. \* A battery replacement or change of generator was done in December, 1975. She returned to Puerto Rico. She did well except for brief bouts of palpitations that resided spontaneously, until February 1976, when after the menses she developed dyspnea, precordial discomfort, moist basilar rales, slight cardiomegaly and changes suggesting congestive heart failure, which were treated with digoxin and fu-

---

*From the Department of Medicine, Section of Cardiology, UPR School of Medicine, Río Piedras, Puerto Rico 00936.*

---

*\*This was done by Dr. Gerald Ryan, Rochester, NY (10), and she probably represents the patient referred to by Dr. Goldstein (1).*



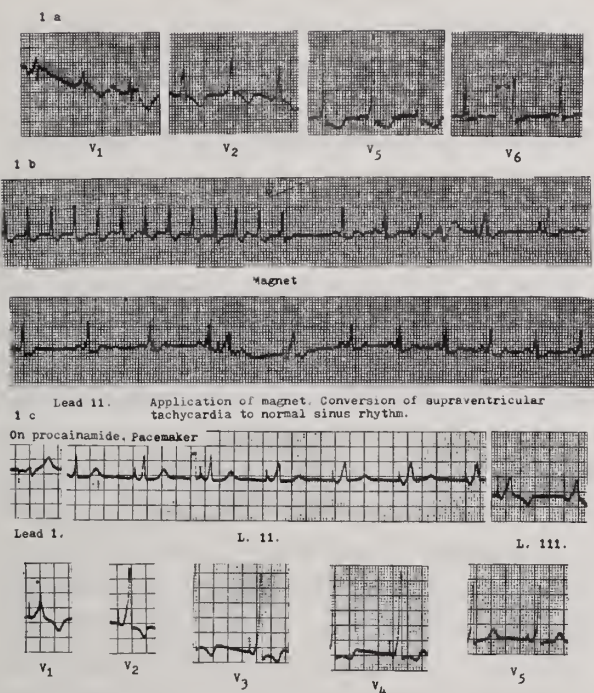


Figure 1. Case 1.

Figure 1

roseamide. The electrocardiogram (ECG) showed a "supraventricular tachycardia" with normal QRS width, rates of 188-231 per minute and ST-T wave changes. After application of a magnet over the generator (right anterior thorax), the rhythm immediately converted to normal sinus without complications (Figure 1 b). A Type A or A-B WPW pattern was revealed (Figure 1 a). She had been advised by her physicians not to apply the magnet herself. She has been maintained since on procainamide (1.25 gms daily), and has been doing well and able to do her housework. Pacemaker-induced beats are conducted with a Type A WPW pattern, as was observed by Preston (Figure 1 c) (12).

#### Case 2:

This is a 50-year-old housewife who has suffered tachyarrhythmias since age 19 years (fifth month of pregnancy). These were sporadic initially, and she even enjoyed 10 asymptomatic years in her early twenties. However, for the last 5 years episodes of tachycardia have become more frequent and severe, and recently have been present much of the time, altering her life

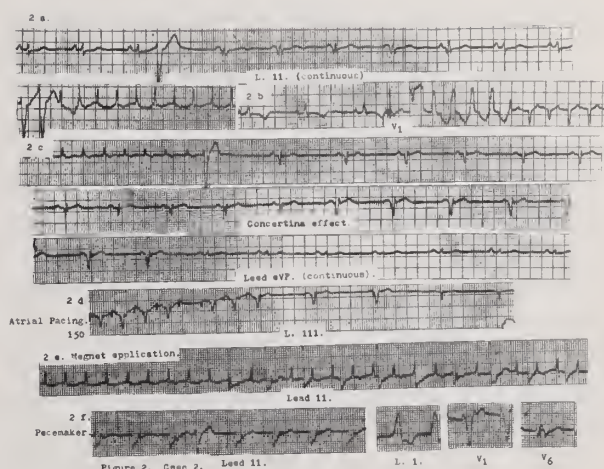


Figure 2. Case 2. Lead 11.

Figure 2

and causing numerous visits to the ER and hospitalizations. Over these last years she has been treated with many different antiarrhythmic medications, singly or in combinations: digitalis, Cedilanid-D, procainamide, quinidine, propranolol, diazepam, reserpine, lidocaine, edrophonium chloride, metaraminol bitartrate, neosynephrine, diuretics and vagal maneuvers with only mediocre success, and indeed, failure to prevent recurrent, and at times almost constant (lasting for days) supraventricular tachycardias (SVT). Failure at times to take the medications, a strong emotional component and heavy family stress have been considered important in her history. ECG's during the tachyarrhythmias always show SVT's (Reciprocating tachycardia) with normal width QRS complexes. Ventricular ectopic beats (PVC's) initiate runs of Reciprocating tachycardia (Figure 2 a, b, c). Occasionally, normal conduction was present; at other times Type A (or a variant) WPW pattern was present (as was seen on the VCG). Atrial ectopic beats (APC's), consecutive PVC's and sinus bradycardia were infrequently noted. So, after failure with all medical therapy and after much discussion with the patient and her family, atrial and right ventricular pacing was performed in the catheterization laboratory. PVC's were suppressed at atrial pacing rates of 80 or greater. Only slight QRS widening occurred, but preexcitation beats were seen when pacing was suddenly discontinued (Figure 2 d). A temporary right ventricular (RV) demand pacemaker with a rate of 90-95 per minute was

placed in the apex. With digoxin, procainamide (2-3 gms daily), propranolol (60-80 mg daily) and the functioning pacemaker, no episodes of tachycardia were detected for a 4 weeks trial period. On the basis of this first success, a RV epicardial, permanent demand pacemaker, rate 90, was placed. Later, at home the patient discontinued the procainamide and propranolol, and the SVT's recurred. Application of a magnet depolarized the ventricles but failed to convert the rhythm (Figure 2 e).<sup>\*</sup> Some evidence of congestive heart failure was present; however, a post-pericardiotomy syndrome was considered likely and prednisone given. Improvement occurred but the heart shadow remains large. On her last admission propranolol was added to the digoxin and procainamide. These multiple medications plus overdrive pacing seems to be presently partially controlling her (Figure 2 f). Pacing and recording from all 4 cardiac chambers, especially the left atrium (LA), would be of greater diagnostic and therapeutic value since she may have a Type A tract, and LA pacing would more likely interrupt the circus movement. Increasing the rate of the pacemaker has been considered; also, we are considering a selective surgical approach, particularly if the newer antiarrhythmic drugs do not become available.

### Discussion

The arrhythmias in the WPW syndrome are usually supraventricular such as atrial and reciprocating tachycardias, believed due to a re-entry circus movement in the atrioventricular (AV) junction and various accessory bypass tracts. Occasionally, atrial fibrillation (Af) or flutter (AF) with aberration (pseudo-ventricular tachycardia), junctional rhythms, AV block, premature atrial and ventricular beats are encountered; rarely are ventricular arrhythmias and other electrocardiographers' delights seen (1, 2, 13).

### Antiarrhythmic Drug Therapy

Antiarrhythmic medications which are often effective solely or in combinations for WPW arrhythmias are digitalis and propranolol which lengthen AV nodal refractoriness, the former

predominately by its vagal action and the latter by its adrenergic blocking action; propranolol usually has no effect on the anomalous pathway and thus may accentuate preexcitation beats (14). They may decrease or abolish the window created by discrepant refractory periods (RP) in the normal and accessory pathways (8). They are ideally suited for tachyarrhythmias with normal width QRS complexes. Procainamide and quinidine lengthen refractoriness or block the bypass tracts (eliminate delta wave), prolong and block ventriculo-atrial (VA) conduction, as well as prevent atrial and ventricular premature contractions which may be incitants of tachycardias; and ideally they are indicated to prevent and terminate Af and AF with wide QRS complexes during the tachycardia, or prevent a fast ventricular response to such. Some authorities believe that digitalis and vagotonic maneuvers are contraindicated in pseudoventricular tachycardia with short RP and rapid conduction over the accessory pathway, as they slow AV transmission time and shorten the bypass RP, aiding faster conduction here, and may induce ventricular fibrillation. Lidocaine shortens or has minimal effect on AV nodal refractoriness but may depress accessory tract transmission. It has converted atrial tachycardia (AT) and Af to normal sinus rhythm (NSR), or has slowed the ventricular response of the latter (15, 16).

Ideal therapy for prevention of SVT should minimize the disparity between refractoriness of the normal and accessory pathways to decrease the chance of a PVC dissociating conduction. A reciprocating tachycardia may be terminated by blocking one of the pathways responsible for the circus movement. Retrograde refractoriness may be quite important and may be the weakest point, as usually the R rather than the retrograde P terminates the paroxysm. Sometimes, however, a trial of all drugs singly, in various dosages and in combinations must be made in attempting to control these difficult arrhythmias (4, 5, 17-19). Other drugs such as prostigmine, neostigmine, amyl nitrite, acetylcholine, phenylephrine,, potassium salts, atropi-

*\*More recently, leaving the magnet in place over the generator succeeded in converting the arrhythmia on at least two occasions.*



ne, reserpine, guanethidine, diphenylhydantoin (has little effect on either pathway), antithyroid drugs and  $^{131}\text{I}$  have infrequently been tried. Excessive alcohol, coffee, tobacco and factors favoring extrasystoles should be avoided.

Ajmaline, verapamil, disopyramide and amiodarone are new antiarrhythmic drugs which are being applied in other countries, but as yet are not FDA-approved for use here or in the U.S. Ajmaline (50 mg IV) prolongs the RP of the accessory tract, but is without effect on the AV node (18). It, as well as B-blockers, procainamide, quinidine and lidocaine may eliminate APC's and PVC's, and be of value in paroxysmal SVT and Af. Verapamil (Cor-dilox, Isoptin) is a calcium ion antagonist that lengthens AV nodal and accessory tract refractoriness. It works against electromechanical coupling, and can convert AT and AF to NSR, and can slow the ventricular rate of Af (20, 21). Disopyramide (Rhydodan) prolongs the transmission time of the anomalous pathway and the effective RP of atria and ventricles. It may be of value in atrial and ventricular arrhythmias, and in Af associated with the WPW syndrome.

Rosenbaum and Wellens have reported impressive results with amiodarone hydrochloride in the prevention and treatment of tachyarrhythmias in WPW syndrome patients when other drugs failed. This is a benzofuran derivative, used as an antianginal agent and which has an antagonistic effect on sympathetic nervous system stimulation. It increases the RP of the AV node, anomalous pathway (AV direction in all and the VA direction in about half), atria and ventricles, and was given in dosages of 100-600 mg/d for 2-8 months. It slows the heart rate of any tachycardia, prevents premature ectopic beats and is especially useful in patients with Af and circus movement tachycardia. It has produced reversible corneal microdeposits (without visual symptoms) and perhaps hypothyroidism; discontinuation for 7 days every 1-2 months was recommended; contraindications are bundle branch block and AV block. It appears promising, and was originally developed by SA Labaz

N.V. from Brussels, and is manufactured in Buenos Aires by Laboratorios Roemmers S.A., under the name of Atlansil (23-26).\*

### Cardiac Pacing

Stimulating, pacing and recording studies are augmenting our knowledge of the electrophysiology of the WPW syndrome. Induced and spontaneous premature beats may initiate and terminate circus movement SVT's; the locations, conduction and refractory properties of the junctional and accessory tracts are being delineated. This information and electrical mapping studies at the time of surgery serve to launch a clinical therapeutic attack upon these recalcitrant arrhythmias (7, 8, 27-32).

Artificial pacemakers have been utilized in the control of various supraventricular and ventricular arrhythmias in general (33-43). They have also proven valuable in the termination and prevention of tachyarrhythmias in the WPW syndrome. A premonition of this was apparent from the early electrophysiological studies and short-term therapeutic interventions, when SVT's were initiated or terminated by the introduction of atrial and ventricular premature beats, or by pacing and paired extrasystoles (27, 44-49).

Their long-term application in this context may be considered under two general aspects: 1) permanent pacemaker for termination of tachycardia; and 2) permanent pacemaker for prevention of tachyarrhythmias. The former was first reported by Ryan & Associates in 1968 in a 52-year old woman with Type A WPW and incapacitating SVT. During an attack a magnet held near the generator changed the pacemaker from a demand to a pre-set fixed-rate mode at a rate of 72 per minute, producing competitive pacing, retrograde atrial depolarization from the RV (260-290 msec after the QRS), with resultant reversion to NSR (10). The patient is alive and well 8 years later. In Preston's patient a permanent LA pacemaker could be turned-on in a fixed-rate mode by application of a magnet (pacing rate of 108), rapidly terminating bouts of tachycardia (12). LA pacing produced WPW

\*Aprendine, Fibocil (Eli Lilly), has shown high success.



Type A complexes suggesting preferential conduction via an abnormal tract, while RA pacing produced QRS's identical to the patient's normal complexes. A radiofrequency RV unit, activated by the Mother to a fixed-rate mode, served in an infant with a Type A tract (50). Recurrent reciprocating tachycardias difficult to control with surgery, in a Type A case, were controlled by a right atrial (RA) scanning pacemaker activated by a magnet (51). A recent success was obtained in a 58-year old male with Type B conduction after multiple drug failure using a RA epicardial lead, a radiofrequency transmitter, antenna and receiver, with external patient activation at a rate of 300 per minute, plus digoxin (52). A total of approximately 24 successful cases have been so treated; the rest had RA, RV or coronary sinus pervenous and LA or LV transthoracic units; the majority were demand, R-wave inhibited units converted to fixed-rate on application of a magnet over the battery-powered pulse generator. Pacemakers were successful in 7 cases not considered optimal candidates for surgery (4, 8). Antiarrhythmic drugs were employed also in some. There were no operative deaths and the long-term survivors were benefited by such pacing (4, 7, 8, 11, 53). Radiofrequency units are used only when the refractory properties of the accessory pathways are known (4).

Paroxysmal repetitive atrial or ventricular discharge has been entertained, and even Af, and ventricular tachycardia and fibrillation are stated to occur not infrequently (11). However, it is stated that this form of therapy is the method of choice for recurring episodes of arrhythmias that would require repeated cardioversion, because it can be performed repeatedly without evidence of heart damage or significant morbidity, especially for WPW patients with frequent symptomatic arrhythmias, and in those patients who are refractory to medications or who decline surgery. The arrhythmias are terminated by interrupting a re-entry circuit (depolarization, reset and depress the tachycardiac pacemaker), rapid overdrive sup-

pression or the initiation of another less stable arrhythmia, such as Af which converts to NSR. Pacing is most successful or requires that the pacing catheter is located fairly close to the site of the accessory tract. Since the route of the circus movement includes a portion of the ventricles, ventricular pacing with retrograde conduction and depolarization of the circus pathway can sometimes interrupt it (4, 8, 40, 49, 51).

Permanent pacemakers to prevent attacks of tachyarrhythmias, as was the primary intention in my Case 2, have also been utilized in both Types A and B patients. Beginning in 1968 with Sowton's patient, some 8 cases have been so managed. Usually demand pacemakers in combination with propranolol or multiple drugs were used, in both children and adults. An epicardial fixed-rate pacemaker was used in a Type B case with AV block, and a demand pacemaker in another case with sinus arrest (54-60). Overdrive atrial and ventricular suppression, prevention of PVC's and changes in diastolic potential, depolarization and threshold are probably the therapeutic mechanisms (27, 49). However, this method may not prevent paroxysmal AF or Af (11).

### Cardiac Surgery

Cardiac surgery for WPW tachyarrhythmias has been applied on an increasing scale in recent years and has achieved impressive but not universal success in otherwise intractable cases, first in Type B with a right-sided accessory bundle and subsequently in Type A cases.

The surgical approach consists of two aspects: 1) surgery on the AV bundle plus placement of an epicardial or pervenous pacemaker; and 2) surgery directed toward one or more aberrant pathways, which are characterized pre-operatively by stimulating and recording studies from the different cardiac chambers, and operative electrical mapping studies (7, 8, 27, 29, 30, 32). Dreifus' Type A patient (61) and Edmonds' Type B patient

(62), with recurrent tachycardias, were controlled by dividing and dissecting the AV node and His Bundle (HB) creating complete AV block. Obviously, this less desirable therapy usually necessitates a prophylactic pacemaker (demand units used), and it is not applicable for WPW cases with Af and fast ventricular responses, as ventricular excitation occurs via impulses over the anomalous conduction pathway. Approximately 15 cases in total have undergone this approach, all Type A except one. Results were good and complete heart block was effectuated in all (by suture, electrocoagulation or transection) with total remission of tachycardiac crises, despite excitation by impulses via the anomalous pathway. One death has occurred. Sealy recommends this approach only in patients with atrioseptal Type A anomalies, as the accessory tract cannot be relied upon to conduct constantly after the block. Wellens recommends it if a Type A pattern exists, if the AV node is an essential link in the tachycardiac circuit and if the RP of the accessory bundle is not very short. For AF and Af, the accessory bundle has to be interrupted. Coumel's patient did not receive a pacemaker (31, 63-69).

The Duke group has pioneered in selective surgery directed toward aberrant conduction pathways. As per their last report about 60 cases including their own patients, in the world, have undergone cutting of an accessory tract (4, 7, 8, 11, 31, 46, 70-81). Burchell et al were the first to attempt such surgery in a Type B case with temporary ablation of the preexcitation (70), but Cobb & associates were the first to succeed (abolished the tachycardia and pre-excitation pattern) in a Type B patient in whom pacing had failed to prevent recurrent tachycardia (71). The age range has been broad, with males and females being about equal. There have been 2 operative deaths and 1 death after discharge.

The Duke experience alone comprises 34 patients. There were 2 operative deaths, and 30

of the 32 survivors are asymptomatic. A breakdown of their figures is as follows: 1) delta gone and no arrhythmias— 19 patients, one of whom died po of low output, 18 asymptomatic; 2) delta gone, arrhythmia persists — 3 patients, retrograde function of AP intact, His section in 2, all asymptomatic; 3) delta unchanged, arrhythmia persists— 2, persistent PAT; 4) delta unchanged, no arrhythmia— 5, 3 required section of HB and 2 easily managed on drugs, all asymptomatic; 5) delta modified, no arrhythmia — 4, all now sensitive to drugs and asymptomatic; 6) no change in PAT - 1, early patient with ? WPW, died po. Tracts have been located in the lateral, anterior and posterior septal RV, in the lateral and posterior LV and atrial septal region; 3 patients had 2 tracts. In their experience septal tracts were more difficult to divide (5 of 14 successful) than lateral free wall tracts (majority successful). Nearly the entire circumference of the mitral and tricuspid rings are incised through the atrial wall at the point of earliest activation, under cardiopulmonary bypass.

Of the remaining group of patients, there has been 1 other death (72), 7 failures (60, 66, 70, 73) and 2 partial successes— delta wave persists, but with a decrease or cessation of arrhythmias (72, 75). Division of the tract was not attempted in one case (48), and tachydysrhythms stopped after only closure of an atrial septal defect in another case (78).

An attempt at surgical interruption of accessory tracts should be considered in selected patients with life-threatening arrhythmias (especially if Af and an extremely fast ventricular response exists), or with disabling tachycardias refractory to medical therapy, and if arrhythmias cause congestive heart failure in patients with underlying heart disease. Section of the HB can be performed if ablation of the accessory tract is not possible, and this will prevent paroxysmal SVT, and possibly episodes of AF if the latter is initiated by re-entry in which the AV node-HB participates (4, 8). A lively discussion as to the relative value of pacemakers versus surgery is

given by Goldstein and Gallagher (11).

As far as is known, these two cases represent the first and only patients with WPW arrhythmias in Puerto Rico in whom pacemakers have been implanted for control of tachyarrhythmias.

### Acknowledgments

To Dr. Jorge A. Carrasquillo, MD, and to other members of the UDH staff for their help in the care of these patients.

*(Readers desiring references may write to the author.)*



## CORONARY ARTERY DISEASE: NATURAL HISTORY, RISK FACTORS AND MANAGEMENT

Henry D. McIntosh, MD and Kinsman E. Wright, Jr., MD

Coronary artery disease is initiated shortly after birth and progresses at a pace that varies from individual to individual and from family to family and from social order to social order. It is uncertain what initiates the process . . . genetic factors . . . environmental factors or other unknown factors.

Coronary artery disease has been demonstrated to have been present centuries ago. Coronary atherosclerosis was present in the mummies found in the pyramids of Egypt. But it has only been in this century that the process has become so common as to be the major cause of death in advanced civilizations. It is now apparent that coronary artery disease is an epidemic.

Epidemiologists have emphasized that the natural history of epidemic diseases, such as typhus, cholera, tuberculosis, pellagra, etc., conform to a basic generalization that is relevant to the consideration of coronary atherosclerosis. Dr. Jeremiah Stamler (1) emphasized that epidemic diseases occur in populations experiencing a confluence of multiple causes that are essential for the massive onslaught of an illness. An epidemic disease rarely has

a single cause, even when there is a clear cut or necessary cause for a given disease. For example, the microbacterium of tuberculosis is the necessary cause of tuberculosis. But it is not a significant cause for the development of the disease to epidemic proportions. The tubercule bacillus has been abroad among human populations for centuries. However, it was not until the 19th century that tuberculosis broke forth as an epidemic . . . the great white plague and the major health problem of the era. The etiologic prerequisites for epidemic tuberculosis were the new social circumstances generated by the industrial revolution. There was a rapid, chaotic expansion of towns into cities with inadequate housing, slums, mass overcrowding, poor sanitation, long hours of fatiguing, dusty, dirty work, child labor and inadequate public health and medical care. These were the multiple socio-cultural factors, the confluence of several causes, which together with the bacteria, produced epidemic tuberculosis. And as these factors were corrected, the epidemic subsided even before the development of drugs and surgery.

Coronary artery disease has, in the course of the 20th century, replaced tuberculosis as the great epidemic of the era in the industrialized countries. Coronary artery disease is the epidemic of a mature, advanced industrial society, as tuberculosis was the epidemic disease of this society in its childhood and adolescence (1).

---

*Current address: The Watson Clinic, Lakeland, Florida.*

*From the Medical Service, The Methodist Hospital, and Department of Medicine, Baylor College of Medicine.*

*Presented as the Conferencia Magistral "Dr. Ramón M. Suárez", on November 20, 1976.*

*This work was supported in part by HL 17269-02 from the National Institutes of Health, U. S. Public Health Services.*

There is now sufficient evidence to indite a confluence of socio-cultural circumstances that are responsible for the emergence of coronary artery disease as the 20th century epidemic of socially advanced countries. These factors include the introduction of cigarettes, the introduction of the automobile and other exercise sparing devices, the increased interest in taste of food, resulting in the addition of salt and increased fat content, the increased incidence of hypertension as a result of salt, nicotine and obesity; the increased stress which is manifested by the separation of patients into Type A and Type B personalities; (2) the increased incidence of diabetes, etc. These are all characteristics of an affluent society. And so the incidence of coronary artery disease reached epidemic proportions.

It became clear in the fifties that there were risk factors which were associated with the development and progression of coronary artery disease (Table I). The relationship between cholesterol and ischemic heart disease in sudden death is well known. The importance of diastolic pressure to coronary artery disease is generally appreciated. As well appreciated is the systolic or casual blood pressure. Similarly cigarette smoking results in an increased

death rate and clinical manifestations of ischemic heart disease. All of these factors when present in the same individual contribute significantly to the mortality from coronary artery disease.

In 1963, Dr. Luther Terry, the Surgeon General for President John Kennedy, based on a careful and detailed study by a committee of experts, reported, "Smoking was dangerous to your health." And so, cigarette packages were labeled. Dr. Terry has recently indicated that, based on data collected about the smoking habits of the American public from 1958 to 1963, that there has been a decline of 20 to 25 million potential smokers (3). It is estimated that one million people in America stop smoking each year. It was estimated that there would have been 75 to 80 million people in America smoking today. In fact, there are only 55 million smokers.

"Eat to live, rather than live to eat", emphasizes the importance of diet. The public has become conscious of its diet. Egg consumption in 1950 was 389 eggs per individual in the United States. Today the consumption is somewhere around 287 eggs per year. It is obvious that the American public is more diet conscious in many other ways as reflected by the popularity of skimmed milk, health foods, etc. Hypertension is better controlled. People are exercising more. What has happened as a result of these changes?

The incidence of death from coronary artery disease, compiled for decades of age, show that there was a gradual increase in the incidence of death from that disease until 1963. This was true for all ages (see Table II). Since 1963 there has been a gradual decline. For the period 1968 to 1974 there has been a decline of 13.6 percent for the white male aged 45 to 54, to 36.6 percent for the non-white female aged 35 to 45 years. The overall death rate in the United States during 1975 declined for the first time to 8.9 deaths per 1,000. This decrease was accounted for in large measure by the continued decline in death from coronary artery disease and from

TABLE I

#### Factors Contributing to the Risk of Coronary Atherosclerosis

- 
1. Genetic factors
  2. Blood lipids
  3. Tobacco consumption
  4. Hypertension
  5. Lack of physical exercise
  6. Emotional stress
  7. Alcohol abuse
  8. Obesity
  9. Diabetes
  10. Decreased lung function
-

TABLE II  
Age-Specific Death Rate from Ischemic Heart Disease  
Per 100,000 Population in the United States

Year	35-44	45-54	55-64	65-74	75-84	85
1958	58.0	232.7	658.4	1,628.8	3,364.8	7,069.3
1959	57.6	233.7	655.3	1,642.6	3,359.2	7,321.0
1960	57.7	238.0	665.5	1,553.7	3,434.8	7,296.5
1961	57.9	235.2	649.4	1,541.4	3,360.6	7,383.3
1962	58.7	238.4	660.4	15,86.7	3,449.2	7,922.2
1963	61.0	240.3	668.4	1,619.1	3,495.6	8,165.6
1964	61.0	235.8	660.3	1,586.7	3,388.6	7,885.7
1965	60.0	236.6	657.4	15,84.0	3,422.0	8,088.2
1966	59.6	236.4	661.4	1,609.9	3,413.6	8,037.7
1967	60.1	231.4	645.0	1,568.8	3,334.2	7,941.8
1968	56.9	216.8	624.1	1,552.2	3,441.7	8,496.7
1969	55.4	210.3	598.4	1,500.3	3,367.6	8,400.2

stroke. These results are not due to coronary care units, surgery or possibly even drugs. They seem to result from changes of a socioeconomic and cultural nature.

It is clear that the incidence of coronary artery disease is increased by factors that can be controlled or modified. If an effort is made by large parts of the population to modify these factors in their own lives, then the incidence of death from coronary artery disease will decline. The physician today must engage in the practice of preventive cardiology.

#### An Overall Philosophy for the Treatment of Coronary Artery Disease

Coronary artery disease is a progressive disease that begins in early childhood. Its management is basically medical (4). Management should consist of emphasizing those therapeutic

modalities and recommendations for changes of life style that are thought to prevent or delay the progression of the disease process; known risk factors must be controlled. As the disease is so common, it is not unreasonable to encourage a universal institution of preventive measures. Every patient, no matter how healthy should be considered a candidate to develop coronary artery disease.

Management should also be directed as is possible within the limits of our present knowledge toward the prevention of the manifestations of ischemic heart disease. These include:

1. pain of angina pectoris
2. myocardial infarction
3. severe arrhythmias
4. premature death
  - a. sudden
  - b. non-sudden



Should an infarct occur, therapy is directed toward minimizing the size of the infarct, minimizing the dilatation of the heart and controlling congestive failure and other complications such as arrhythmias, ventricular septal defects, rupture, mitral insufficiency, aneurysm, etc.

Surgery has a major role in the treatment of some of these complications of a myocardial infarction. Surgery is the only way to repair a ruptured septum or a ruptured papillary muscle or chordae tendineae. It may be desirable to resect an aneurysm or dyskinetic area of the myocardium. Very rarely, surgery may be useful in the treatment of arrhythmias due to conduction abnormalities, or the persistence of an irritable foci which may produce life threatening arrhythmias.

Surgery is most useful in the control of pain of myocardial ischemia that is not responsive to medical measures and which interferes significantly with the quality of life. To date, the data are not conclusive that coronary bypass surgery will prevent sudden death or prevent myocardial infarction, or prolong life except in selected subsets of patients. There is evidence that coronary bypass surgery may, in some patients, accelerate the basic atherosclerotic process (4).

At this stage of our knowledge, there is little benefit to be gained from documentation of symptomatic or minimally symptomatic stable coronary artery disease by coronary arteriography. That coronary artery disease is present in a middle aged male, can almost be assumed in most patients. The radiographic documentation of coronary artery disease does not permit one to accept that the process is the cause of a specific symptom, in most cases. In the individual patient, coronary arteriography has little value in predicting prognosis.

The natural history of coronary artery disease may be likened unto an iceberg: eight-ninths of the ice is below the surface of water, one-ninth above. Asymptomatic coronary artery disease is like that part of the iceberg below the surface of the water; symptomatic coronary ar-

tery disease is represented by that part above the water. When coronary artery disease becomes symptomatic, it should be referred to as ischemic heart disease. Ischemic heart disease is best demonstrated by a careful history with or without ischemic changes of the electrocardiogram and/or the appearance of classical changes in the physical examination of the heart at the time that pain is present. The mere demonstration of coronary artery disease by coronary arteriography does not establish the diagnosis of ischemic heart disease. In returning to the analogy of the iceberg, the demonstration of coronary artery disease by coronary arteriography does not permit the physician to state whether the patient should properly be placed in that portion of the iceberg above the surface of the water, i.e. ischemic heart disease, or below the surface of the water, i.e. asymptomatic coronary artery disease.

When the symptoms of angina pectoris cannot be controlled medically so as not to impair the desired quality of life, the physician and the patient may wish to consider the incorporation of coronary bypass surgery into the medical management of the progressive disease. Under such circumstances, knowledge as to the precise location of the lesions and their severity, the state of the distal vessels and the contractility of the myocardium is needed in order to determine the likelihood of improvement by surgery. This knowledge is only determined by high quality, carefully interpreted arteriograms. At this time, in the progressive course of coronary artery disease, coronary arteriography is usually indicated in most, but not all, patients for the first time. Occasionally coronary arteriography is also indicated to settle diagnostic dilemmas, especially in the presence of conduction abnormalities demonstrated on the electrocardiogram. It may also be indicated in the preoperative assessment of patients with valvular heart disease if angina pectoris is present. It also is of use as part of an investigative study in the postoperative evaluation of patients who have undergone bypass surgery, or those patients who have not responded as expected to the sur-

gical procedure.

Coronary arteriography is not indicated simply to establish the presence or absence of coronary artery disease. This does little but expose the patient to unnecessary hazards, such as excessive radiation, a compromise of a peripheral artery that may be needed at a later time and occasionally death. It also creates a significant financial burden for the patient.

Similarly, coronary artery bypass surgery is not indicated merely for the presence of coronary artery disease. Its main use is in the treatment of the pain of ischemic heart disease that cannot be controlled medically that is interfering significantly with the quality of life. There is evidence to suggest that bypass surgery may prolong life in the small subset of patients with left main coronary artery stenosis (5) and possibly those patients with significant stenosis of three vessels and normally contracting ventricles. It may also prolong life in patients who develop ischemic changes during stress electrocardiography at low levels of exertion (i.e. 3 to 4 minutes) and who have proximal lesions with normally contracting ventricles. The effect on survival of this group of patients, however, is yet to be defined.

#### The Evaluation of the Patients Suspected of having Coronary Artery Disease

The management of coronary artery disease begins with a careful history. Is angina pectoris present? A careful assessment of the smoking habits, personality and exercise tolerance should be carried out as well as a careful family history.

A careful physical examination is then indicated. The blood pressure is probably the most crucial assessment in the otherwise well individual. Casual blood pressure determinations are more representative of what the blood pressure really is than is a basal blood pressure determination. The physician is more interested in what

the blood pressure is, under stress, than what it is at rest. The physician wants to know how high the blood pressure goes, rather than how low it goes.

Contrary to popular clinical folklore, there is little evidence that the serious consequences of hypertension result entirely from the diastolic component of the blood pressure. Systolic pressure predicts just as well as diastolic for every major cardiovascular problem to which hypertensive patients fall heir. There is no evidence that evaluation of systolic pressure is an innocuous accompaniment of aging. Risk gradients for systolic pressure do not wane with advancing ages (6). There is no evidence to support the contention that women in general and post menopausal women in particular tolerate hypertension well. They may tolerate it better than men, but not well. It is not hypertension that predisposes to cardiovascular disease but the degree of elevation of the blood pressure. There is no critical hypertensive value.

The next most important consideration is whether there is evidence of cardiac enlargement or hypertrophy and whether or not the patient is obese, not massively obese but even minimally so.

In evaluating obesity, the skin fold thickness is a much better measure of obesity than the absolute weight. The thickness of the skin folds should be measured lateral to the umbilicus, under the triceps of the forearm and in the infrascapular region of the back. Calipers are more precise but this measurement can easily be estimated by careful observation. The total thickness at these three sites should not exceed one and a half to two inches in the nonobese individual (7).

The routine laboratory should include the two hour P.C. sugar, cholesterol, triglycerides, uric acid, an electrocardiogram and a chest x-ray.

Having obtained the history, carried out the physical examination and obtained the routine laboratory data, it is important to define the individual risk factor profile (Table III).

The concept of "normal" should be distin-



TABLE III

## Individual Risk Factor Profile

---

I.	Personal atherogenic attributes
1.	Blood pressure
2.	Serum cholesterol and triglycerides
3.	Glucose intolerance
II.	Living habits that promote above traits
1.	Inactivity - sedentary existence
2.	Overeating - obesity
3.	Cigarette smoking
III.	Signs of preclinical disease
1.	ECG abnormalities
2.	Cardiac enlargement on x-ray
3.	Other evidence of impaired function

---

guished between usual and ideal. There is no critical hypertensive value. Its effect is progressive. There is no discernable critical value for cholesterol, lipoprotein, carbohydrate tolerance, overweight or obesity. The normal range of cholesterol values reported by most laboratories, i.e. 150 to 250 mgs/per cent, embrace a five fold increased risk of coronary artery disease. A patient with a cholesterol level in the upper limits of normal is statistically five times more likely to have significant coronary artery disease in a patient with a cholesterol at the lower limits of normal.

The resting electrocardiogram has a predictive value. The preclinical stage of ischemic heart disease can be predicted with reasonable accuracy when the ECG findings of left ventricular hypertrophy, non-specific ST and T wave changes and/or IV conduction defects are present, plus one other risk factor. The presence of electrocardiographic changes or myocardial infarction, even without history, indica-

te evidence of coronary artery disease. Almost one in four myocardial infarcts is silent.

## The Education of the Patient About Coronary Artery Disease

A basic consideration in the overall management of the patient with coronary artery disease, either in the clinical or pre-clinical phase, is to get the patient to understand the disease process and the significance of the pain of angina pectoris. Coronary atherosclerosis can be explained by the analogy of a lake on a farm. Although, there may be much water in the lake, it is not helpful to the crops if irrigation ditches are not dug. In extremely hot weather, if an irrigation ditch becomes obstructed with trash, the affected crop will wither. The withered plants are analogous to ischemic heart cells. If a cloud appears and removes the stress, i.e., the heat of the sun, up to a certain point the crop recovers, if not, it dies. This is analogous to a myocardial infarction. The analogy can be extended to incorporate the concept of the development of collaterals or bypass surgery or other aspects of therapy. The educated person is a more cooperative person and understands his disease and the reasons why he should follow therapy.

## The Management of Coronary Artery Disease

Control of the blood pressure is a prime objective in managing patients with coronary artery disease. The goal is to maintain the lowest possible blood pressure without producing side effects. There are several factors which contribute to hypertension that can be modified by nonpharmacologic means. The chief of these is excessive sodium intake. The patient should be urged to form a "no-salt added" habit. In addition, the patient should avoid excessively salty foods. Smoking contributes to an elevated



blood pressure in many patients. Obesity can also contribute to an elevation. If after control of the sodium intake, smoking and weight, the adult patient consistently has a systolic blood pressure in excess of 140 mm. of mercury, then drugs should be added. A diuretic will be all that is required by most patients to control the blood pressure. The minority will require additional drugs. If the management is difficult the patient should be supplied with a blood pressure cuff so that he or she can become involved actively in the drug regulation. Such a practice increases patient compliance. It hardly seems less complex to control insulin levels than antihypertensive agents. Patients for years have adjusted insulin levels.

The second objective is control of weight. As indicated, this is best done by evaluating the skin fold thickness. The patient should, however, be urged to weigh each day and record the weight. The most important aspect of weight reduction is control of calories. If cholesterol and triglycerides are elevated, added restrictions are indicated.

It has been shown that there is a relationship of even slight excesses of weight with the cholesterol, systolic blood pressure, blood glucose and uric acid levels. Furthermore, it has been shown that being underweight reduces the level of these parameters below what is considered normal. Even slight obesity increases the risk of experiencing coronary event. The treatment of obesity is difficult but it is essential.

If cholesterol is still abnormal after weight reduction, or if it is desired to take advantage of the lowest possible cholesterol level, then diet modification should be added. The main thrust is to reduce the saturated fat, and when possible, increase the unsaturated fat. About 27 percent of the calories should come from unsaturated fat sources and 13 percent from saturated fat. The patient should be encouraged to eat red meat, i.e. pork, beef, lamb and veal once a week; chicken without skin or visible fat and fish can be eaten ad lib. The patient should avoid cheese, whole milk or hard margarine or butter. Substitute cheeses are now

finding their way to the markets and skimmed milk and tub margarine which cannot be hardened into blocks, is quite satisfactory.

If after such precautions, the cholesterol is still above the desired level, then institution of drugs should be considered. Cholestyramine is effective, but it invariably results in bothersome constipation. This can be relieved with a stool softener. Nicotinic acid is also effective. The drug should be started in small doses of 200 mg. t.i.d. and gradually increased as the patient develops a tolerance. Dextrothyroxine is also said to be effective but if overt coronary artery disease is present, propranolol should be administered first to allow the heart rate and to control it. With such a precaution, this drug can be tolerated by most patients with angina pectoris.

Hypertriglyceridemia can be modified by diet mainly by controlling calories and alcohol. If after such restrictions, the triglycerides are still elevated, drugs such as clofibrate and nicotinic acid may be useful.

The cholesterol and triglycerides should be checked frequently, that is a week after a diet change or a change in medicine. The patient should know and record the results. The patient should be compulsive about weight, skin fold thickness, blood pressure determination, cholesterol and triglycerides, etc. The patient should keep an accurate record of all of these determinations.

Now in the treatment process, attention must be directed to smoking. It is encouraging to note for those who renounce the habit (except for those over the age of 65), the risk is half of those who continue to smoke. There is no safe cigarette as far as coronary artery disease is concerned. Low tar, low nicotine still have a high carbon monoxide content. Carbon monoxide is thought to be the major offending agent contributing to coronary artery disease.

Finally, the activity of the individual is important. There is no evidence that excessive exercise is essential or even beneficial in reducing coronary artery disease. The average American exercises below the minimum level required

to prevent coronary atherosclerosis, however. The physician must prescribe a specific exercise program. Walking, swimming, jogging or bicycling are all excellent. Care should be exercised in recommending a competitive sport such as tennis if ischemic heart disease is present. The exact exercise prescription will depend on the performance of the patient on a carefully monitored stress test. The Committee on Exercise of the American Heart Association has recently published an excellent booklet on exercise testing and training of apparently healthy individuals (8). There is a second booklet also available regarding patients with known ischemic heart disease (9). Finally, one should recommend jogging cautiously and be aware of the possibility of exacerbating silent orthopedic problems. After a gradual increase in duration and speed, one gains an insight into the patient's ability to jog without developing complications.

Regardless of the infrequency of the episodes of angina pectoris or its mildness, the patient should always carry sublingual nitroglycerin. The drug, once the bottle is opened, deteriorates rapidly . . . over a three month period. It should be discarded and a fresh supply obtained every three to four months. The drug should be carried in a dark glass bottle with only a pledget of cotton in the top under a tight fitting cap. It should not be carried with other medications. The patient should be encouraged to take the medication at the first sign of pain and also as a prophylaxis if certain physical stresses are frequently associated with pain. The patient that is thought to be "refractory to medical management" frequently is not using nitroglycerin properly.

If angina persists and is frequent after such a program, then more specific pharmacologic agents are indicated. A long acting vasodilator, such as isosorbide dinitrate, 5 to 10 mg. sublingually q. 3 to 4 hours, is effective when combined with propranolol in sufficient dose to maintain at rest a heart rate of 60 to 70 beats per minute. Arrhythmias are cause for concern and treatment must be individualized.

They frequently will be reduced by control of hypertension, cigarette smoking and reduction of coffee and allaying of anxiety.

If one cannot control the pain of angina pectoris, then a consideration of surgery is indicated. When surgery is considered, one should realize what is currently known about the results of bypass surgery. What is known about the operation can be summarized as follows:

1. 80 percent or more of the grafts to the left anterior descending coronary artery will be in many centers, be patent for periods up to five years. Patency to the circumflex coronary artery probably is not as good.
2. 70 to 80 percent of the patients can expect relief from angina; 50 percent of the patients will have improved tolerance to stress testing.
3. Improved myocardial contractility is demonstrated only in about 25 percent of the patients in whom contractility was demonstratively depressed.
4. It is not known whether the procedure prolongs life. The data strongly suggests that it does in patients with critical stenosis of the left main coronary artery and possibly three vessel disease. There is no evidence that it prolongs life in a broad group of patients presenting with a picture of unstable angina.
5. The incidence of perioperative myocardial infarction is unfortunately high, 10 to 15 percent in most centers.
6. There is no evidence that the procedure prevents sudden death.
7. There is evidence that the procedure accelerates the disease process in the native circulation. Certainly, this is true as far as that portion of the artery is proximal to the graft. The effect as far as the acceleration of disease in the artery distal to the graft is at the present time not clear.
8. Except for relief of pain, there is no definitive evidence that the procedure alters the course of coronary artery disease favorably, except in carefully selected sub-



sets of patients such as those with high grade stenosis of the left main coronary artery.

In addition, there is a definite operative mortality which varies from institution to institution and may be anywhere from one to seven percent. Twenty-five percent of patients do not return to gainful employment after bypass surgery and 30 percent of a group of patients changed employment after surgery (10). These patients were 55 years and older. The evaluation and operative procedure costs between \$10,000 and \$15,000. It also is important to note that there is a marked variation in the surgical skill from institution to institution and in the same institutions.

Specifically, there is no justification in view of the above considerations for bypass surgery in the patient with asymptomatic coronary artery disease. It is not indicated in the patient with stable angina pectoris in whom the clinical manifestation of disease can be readily controlled. It is not indicated for the vast majority of patients with the intermediate syndrome. Certainly these patients do not pose an indication for emergency evaluation and surgery. Time can be taken to stabilize the patient to be certain that they are not suffering from an acute myocardial infarction. The patient with the Prinzmetal syndrome of angina pectoris does not respond as well to bypass procedures as do patients with more classical forms of angina. There is little indication for considering bypass surgery after an uncomplicated myocardial infarction in the patient that becomes asymptomatic. Certainly surgery is to be avoided in the patient with the acute myocardial infarction. Its role in the management of patients in conjunction with the intraaortic balloon in patients with cardiogenic shock is still under consideration.

At all stages of the clinical manifestations of the disease, rehabilitation is essential. The

patient should be encouraged to develop an optimistic attitude. He should be made aware that he can modify the course of the disease by watching his personal habits.

This then is an overview of the philosophy regarding management of coronary artery disease. This disease is not a surgical disease but is a medical disease in which surgery is sometimes used. Not only does the physician need to make recommendations regarding specific therapy, he must also emphasize to his patients the importance of preventive cardiovascular disease. These are things that the physician must do for each patient. Surgery is indicated, but only when the pain is refractory or when a left main stem lesion has been demonstrated.

## References

1. Stamler, J., Berkson, D. M., Lindberg, H. A.: Risk factors: Their role in the etiology and pathogenesis of the atherosclerotic diseases. *Pathogenesis of Atherosclerosis*. Edited by Weissler, RW, and Gur, JC. Baltimore, The Williams and Wilkins Co., 1972.
2. Friedman, M. and Rosenman, R. H.: *Type A Behavior and Your Heart*. Alfred A. Knopf, 1974. New York.
3. Luther Terry: Personal communication.
4. McIntosh, H. D., Wright, K. E. and Wray, N. P.: Indications for saphenous vein aortocoronary bypass surgery. *Atherosclerosis Reviews* 1:183, 1976.
5. Lin, J. S., Proudfit, W. L., Sones, M.: Left main coronary arterial obstruction: Long term follow-up of 141 surgical cases. *Am J Cardiol* 36: 131, 1975.
6. Veterans Administration cooperative study group on anti-hypertensive agents. *JAMA* 213: 1143, 1970.
7. Whyte, H. M.: Behind the adipose curtain: Studies in Australia and New Guinea relating to obesity and coronary artery disease. *Am J. Cardiol* 15: 66, 1965.
8. Kattus, A. A. and members of the Committee on Exercise, American Heart Association. *Exercise Testing and Training of Apparently Healthy Individuals: A Handbook for Physicians*. 1972 Dallas, Texas.
9. *Ibid*: *Exercise Testing and Training of Individuals with Heart Disease at High Risk for its Development: A Handbook for Physicians*. 1972 Dallas, Texas.
10. Rimm, A. A., Barboriok, J. J., Anderson, A. J., and Simon, J. S.: Changes in Occupation after aortocoronary vein bypass operation. *JAMA* 236: 361, 1976.



## DIAGNOSTIC X-RAYS DECLARED HARMFUL

Chicago — The dialogue among medical experts regarding possible genetic harm from low doses of diagnostic X-rays continues in the May 30 Journal of the American Medical Association.

A study by Irwin D. J. Bross, Ph.D., and N. Natarajan of Roswell Park Memorial Institute, Buffalo, concludes that "there is clear prima facie evidence that exposure to the low levels of ionizing radiation can produce a drastically increased risk of leukemia and other diseases in the children of persons exposed to these levels." The incidence of leukemia in recent years is 21,00 per year.

For the minority of exposed persons (about 1 percent) who are affected by the radiation, there is a 50-fold increase in the risk of leukemia and a five-fold increase in certain other diseases, Dr. Bross reports.

"These findings refute a dogma that is often cited by radiologists who claim that diagnostic radiation is harmless," he declares.

In commenting on the Roswell Park study, medical authorities pointed out that benefits from low dosage diagnostic X-rays, which can determine in advance many serious medical problems related to childbirth, are substantial, and benefits must be weighed against risk.

Damage from X-ray appears in 1 percent of the children in the study.

It has been assumed that genetic damage is virtually eliminated by a process known as fractionation, in which the total dose of radiation is administered in small doses at intervals. But, says Dr. Bross, "genetic damage still occurs even with fractionalization."

"Fractionalization creates the illusion that the genetic damage has disappeared, when, in actuality, the genetic damage to the population is, if anything increased."

When a mother is exposed to radiation during pregnancy, genetic damage occurs in only a small proportion of babies. This damage will later be expressed as increased risk of certain childhood diseases. Diseases in addition to leukemia are asthma, skin rash, eczema,

pneumonia, dysentery, and rheumatic fever, he says.

## AMA ANNOUNCES \$5,000 GRANT FOR JOURNALISM FELLOWSHIPS

Chicago — The American Medical Association has awarded a grant of \$5,000 to the Council for the Advancement of Science Writing in support of the Nate Haseltine Fellowship Program in scientific writing.

The grant will provide fellowships of up to \$1,500 a year to working journalists and journalism students who wish to pursue a career in science writing.

The fellowship program replaces the AMA's 13-year Journalism awards program in which awards totaling \$5,000 each year were presented for outstanding reporting and writing on the science and art of medicine.

The new fellowship program will continue the AMA's interest in supporting American journalism that contributes to a better understanding of medicine and health, declared James H. Sammons, M. D., AMA executive vice president, in announcing the award.

The program will be administered by the Council for the Advancement of Science Writing. Application blanks and further information are available from William J. Cromie, executive director, CASW, 618 N. Elmwood, Oak Park, Ill. 60302.

The program is named in honor of the late Nate Haseltine, long time leading American science writer. Working journalists with two years or more of experience who wish to specialize in science writing or to upgrade their skills may apply. Journalists working full-time can apply for fellowship funds for part-time schooling or self-directed study. The study program would involve working with an experienced science writer and receiving funds for reference materials and travel to scientific meetings.

Students applicants must have undergraduate degrees in journalism or science and prove to the satisfaction of a selection committee that they have the motivation and ability to become science writers.

$\frac{20}{150}$

# H

$\frac{20}{100}$

# E A R

$\frac{20}{70}$

# I N G I S

$\frac{20}{50}$  A S P R E C I O U S

$\frac{20}{40}$  A S S I G H T H A V E

$\frac{20}{30}$  Y O U H A D Y O U R H E A R I N G

$\frac{20}{20}$  T E S T E D L A T E L Y A S I M P L Y

$\frac{20}{15}$  C O M F O R T A B L E H E A R I N G

$\frac{20}{10}$  I N V E S T M E N T O F A F E W M I N U T E S

Hearing losses are among the most consistently neglected health problems. Many people with them won't even admit it to themselves, let alone others. A little encouragement may start them thinking about themselves more realistically.

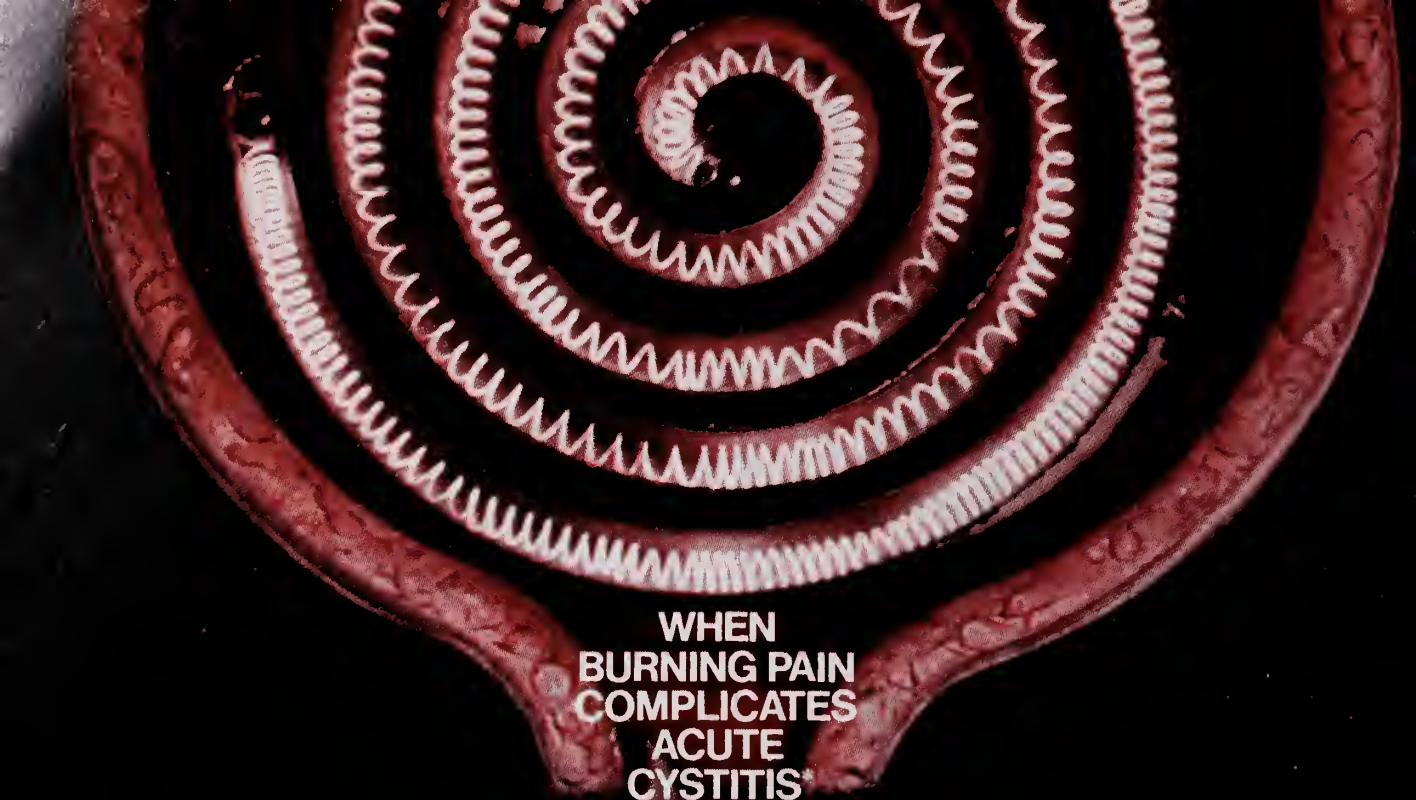
That's why we're offering you the poster shown here. You can hang it on the wall or stand it on a small table. It comes with booklets called "As precious as sight" that give your patients some basic facts about auditory testing and hearing losses and how easy they are to correct in many cases.

Write to us for your free poster and booklets. They just might help you to help some patients who aren't hearing as well as they used to. Even those who ordinarily wouldn't hear of it.

Professional Relations Division, Beltone Electronics Corporation  
4201 West Victoria Street, Chicago, Illinois 60646, an American company

***Beltone***  
WHEN A HEARING  
AID WILL HELP





WHEN  
BURNING PAIN  
COMPLICATES  
ACUTE  
CYSTITIS\*

TURN IT OFF WITH

# AZO GANTANOL<sup>®</sup>

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

## FOR THE PAIN

- Quickly relieves painful symptoms such as burning and pain associated with urgency and frequency
- Recommended antibacterial therapy up to 3 days with Azo Gantanol, then 11 days with Gantanol (sulfamethoxazole).

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies

**Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels as variations may occur, 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma, in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura,

## FOR THE PATHOGENS

- Effectively controls susceptible pathogens such as *E. coli*, *Klebsiella-Aerobacter*, *Staph aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

\*nonobstructed due to susceptible organisms

hypoprothrombinemia and methemoglobinemia), allergic reactions (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis), *G I reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis), *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist

**Dosage:** Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**NOTE:** Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



# DYAZIDE<sup>®</sup>

Trademark

Each capsule contains 50 mg. of Dyrenium<sup>®</sup> (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE FOR LONG-TERM CONTROL OF HYPERTENSION\*



**LOWERS  
BLOOD  
PRESSURE**

**CONSERVES  
POTASSIUM**

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### **\* WARNING**

This fixed combination drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**\* Indications:** When the fixed combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium-sparing action of its 'Dyrenium' component is warranted.

**Contraindications:** Further use in progressive renal or hepatic dysfunction; hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs. Routine use of diuretics in otherwise healthy pregnancy.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with

cardiac irregularities. It is more likely in severely ill patients with urine volume less than one liter/day, the elderly or diabetics, with suspected or confirmed renal insufficiency. Periodic determinations of serum  $K^+$  should be made. If hyperkalemia develops, substitute a thiazide alone, restrict  $K^+$  intake. The presence of a widened QRS complex or arrhythmia in association with hyperkalemia requires prompt additional therapy. Thiazides are reported to cross the placental barrier and appear in breast milk; fetal or neonatal hyperbilirubinemia, thrombocytopenia, altered carbohydrate metabolism and other adverse reactions that have occurred in the adult may result. When used in pregnancy or in women who might bear children, weigh potential benefits against possible hazards to fetus. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics, or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spiro-lactone is used concomitantly, determine serum  $K^+$  frequently; both can cause  $K^+$  retention and elevated serum  $K^+$ . Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving Dyrenium<sup>®</sup> (triamterene, SK&F Co.), and

leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Do periodic blood studies in cirrhotics to check for nondrug-related variations in blood pictures, and in patients with folic acid depletion, since 'Dyrenium' may contribute to appearance of megaloblastosis. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine.

**Adverse Reactions:** Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

**Supplied:** Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

**SK&F CO.,** Carolina, P.R. 00630  
Subsidiary of SmithKline Corporation

## TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE



**BURROUGHS WELLCOME CO. MAKES  
CODEINE COMBINATION PRODUCTS.  
YOU MAKE THE CHOICE.**



**EMPIRIN<sup>®</sup>  
COMPOUND  
̄ CODEINE  
#3**

Each tablet contains:  
codeine phosphate, 32 mg (gr ½),  
(Warning: May be habit-forming);  
aspirin, 227 mg; phenacetin, 162 mg;  
and caffeine, 32 mg.



**EMPRACET<sup>™</sup>  
̄ CODEINE  
#3**

Each tablet contains:  
codeine phosphate, 30 mg (gr ½),  
(Warning: May be habit-forming);  
and acetaminophen 300 mg.



**Burroughs Wellcome Co.**  
Research Triangle Park  
North Carolina 27709

*PREVENTION OF FOOD POISONING IS GOAL OF NEW AMA PAMPHLET*

CHICAGO — Food poisoning makes a lot of Americans very sick each year. Most of it is unnecessary.

Salmonella infection alone is estimated to affect more than a million Americans each year. It brings diarrhea, severe stomach pains, vomiting and fever. It is seldom fatal but is highly uncomfortable for a day or two.

The nation's foremost food hazard continues to be microbial food poisoning, says a new pamphlet on foodborne illness from the American Medical Association.

And the major cause is faulty food-handling practices in the home and in public eating places, the AMA says. The number of outbreaks indicates clearly that many consumers know too little about the prevention of foodborne illness.

The pamphlet describes four major types of food poisoning and offers suggestions on how to avoid it.

Salmonella organisms are found most frequently on raw animal products — meats, poultry and eggs. Refrigeration and freezing retard their growth and cooking destroys the organisms. To prevent growth and spread of Salmonella — use hot, soapy water to wash hands, utensils, cutting boards or counter tops that have been in contact with raw meats, poultry and eggs; thaw frozen meats in the refrigerator, not at room temperature; do not stuff poultry until just prior to cooking, and use a meat thermometer to make certain the fowl is thoroughly cooked; refrigerate leftovers promptly and heat them thoroughly before serving; use clean eggs without cracked shells.

To prevent illness from *Staphylococcus aureus* organisms — do not keep foods at room temperature or at warm holding temperatures; do not use hands to mix foods, and keep hands away from mouth, nose and hair; any person with a skin infection or infectious disease should not prepare food. The staph toxin,

unlike bacteria, is not destroyed by cooking. Foods that support the growth of staph organisms are ham, cream-filled pastries, custard, egg dishes, gravies, stuffing and meat and poultry dishes.

Cooked meat and poultry dishes and gravies also may harbor *Clostridium perfringens* spores. Abdominal cramps and diarrhea develop about 10 to 12 hours after eating. Prevention involves frequent washing of hands while preparing food, prompt refrigeration and thorough reheating of leftovers, and care to avoid cross contamination, as in Salmonella.

The most serious food poisoning is caused by a bacterium known as *Clostridium botulinum* — Botulism. Botulism is rare, but often is fatal. The major cause is eating improperly processed, home-canned vegetables. It results in double vision, inability to swallow, speech difficulty, and progressive respiratory paralysis.

To prevent Botulism — use only the pressure-canner method of canning vegetables, meats or poultry at home, obtain reliable canning instructions, such as those available from the U. S. Department of Agriculture; throw out foods with odd odors; do not even taste food that is suspect; if doubtful, boil meats, poultry, corn or spinach for 20 minutes and other vegetables at least 10 minutes; discard cans that leak or bulge.

If foodborne illness strikes, call your doctor, and wrap up and label samples of the suspect foods for possible laboratory analysis by health authorities.

The pamphlet — "Foodborne Illness: The Consumer's Role in Its Prevention," was prepared by the AMA's Department of Foods and Nutrition.

---

*NEW GUIDELINES OFFERED FOR X-RAYS OF BREAST*

CHICAGO — Recent publicity about potential



dangers of mammography screening has generated an emotional reaction in both lay and professional circles. Mammography means X-ray of the breast to determine whether cancer is present. Use of diagnostic X-ray when indicated is not in question. The problem comes in the mass screening by X-ray of women who have no symptoms and are not in the high risk groups.

The danger comes from the possibility that the X-ray itself may cause cancer.

American women and often their physicians as well are in a quandary over whether to use X-ray to check for cancer.

There still are some unknown factors in this situation, but, given the present state of medical knowledge, some practical guidelines for mammography are offered in the March 7 Journal of the American Medical Association by researchers from the Scripps Clinic and Research Foundation, LaJolla, California:

1. Any woman, regardless of age, with signs or symptoms that indicate breast cancer (such as a lump) should have a mammograph.

2. A woman who has a high risk for breast cancer (strong family history, previous breast cancer, no pregnancy before 30 years of age) should receive periodic screening examinations, including mammography.

3. Periodic screening should be done for all women over the age of 50 years.

4. Women under 50 years without symptoms should not be screened until further facts are discovered on the benefits and risks.

---

#### NEW CRITERIA LISTED FOR BRAIN DEATH

CHICAGO — Criteria for determining when the brain is truly dead, even though machines may be keeping the heart beating and the lungs breathing, are listed in the March 7 Journal of the American Medical Association.

The National Institute of Neurological and Communicative Disorders and Stroke sponsored a study in which 503 patients were examined in nine medical centers.

The study concluded that establishment of cerebral death requires:

1. All appropriate examinations and treatment procedures have been performed.

2. The brain is completely unresponsive, breathing without the machines has stopped, pupils are dilated, reflexes such as blinking are missing, and the electrocardiogram is silent for 30 minutes at least six hours after the stroke or accident.

3. If one of these standards is met imprecisely or cannot be tested, a confirmatory test be made to demonstrate the absence of blood flow in the brain.

The third rule would allow the diagnosis of a dead brain to be made in patients with small amounts of sedative drugs in the blood, in patients undergoing treatment procedures that make examination of cranial nerves impossible, and in patients otherwise meeting the criteria but whose pupils are not dilated.

Project coordinator for the study was A. Earl Walker, M. D., of the University of New Mexico School of Medicine, Albuquerque.

The state known as brain death came to the attention of physicians and the public some years ago when transplant surgery gained popularity. Viable organs were needed for transplant. If the pronouncement of death was delayed until the heart stopped beating, the organs underwent so much deterioration that a successful transplant was jeopardized, Dr. Walker points out.

Dr. Walker distinguishes between brain death and irreversible coma. Brain death means total destruction of the brain. Irreversible coma refers to a vegetating state in which all functions attributed to the brain are lost, but certain vital functions, such as respiration, temperature and blood pressure regulation may be retained.

Legal statutes in a number of states recognize brain death but not irreversible coma as a means of certifying death.

# OFICINAS de RENTA:

Después de un abarcador estudio hecho por Health Management Associates, Inc. que preside Ramón L. Rosario, MHA, el local que más adelante describiremos fue elogiosamente recomendado para el establecimiento de oficinas médicas o grupos médicos, ya que la zona es una de mejor rendimiento económico del área, existe una escasez tal de servicios para algunas especialidades que los necesitados tienen que procurarla fuera del área, por las condiciones del edificio con más de 120 espacios de estacionamiento con entradas por las Calles Loíza, McLeary y María Moczó.

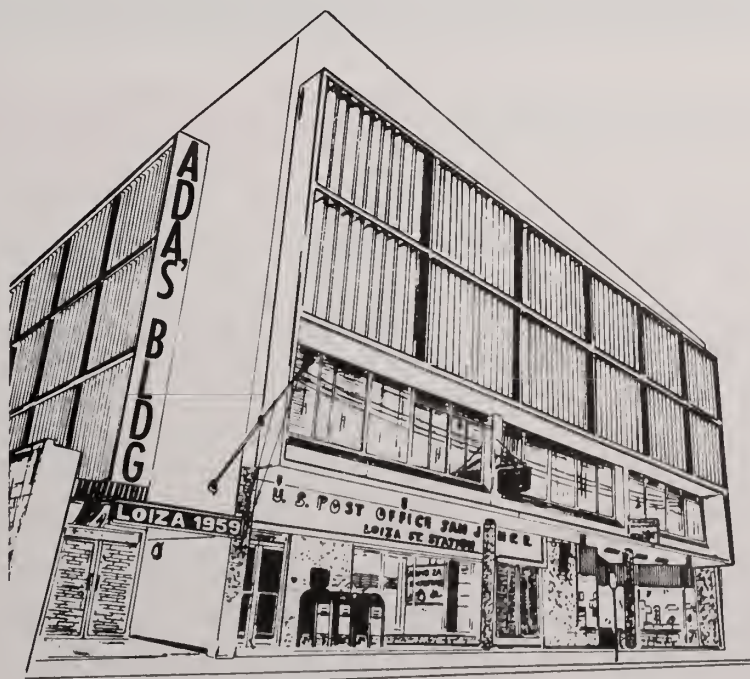
El edificio está localizado de tres a cinco minutos del Hospital Presbiteriano, Hospital San Jorge, Professional Hospital, Clínica Mimiya, Ashford Medical Center y Centro Gubernamental Minillas. A diez minutos de la zona hotelera del Condado, Isla Verde y el Aeropuerto Internacional. Hay servicio de transportación pública para el pueblo y todos los barrios de Carolina que enlazan con el servicio de la Autoridad Metropolitana de Autobuses.

Más de 20,000 pies cuadrados disponibles y adaptables a las necesidades del profesional.

Creemos que lo ofrecido es el sitio ideal para el profesional agresivo que procura un buen futuro.

A todo aquel interesado podemos darle toda la información bosquejada en los párrafos anteriores así como nuestro deseo de cooperar en la preparación de una oficina de acuerdo con las necesidades de la especialidad profesional.

Para información favor de llamar al Sr. Claudio Ugarte, teléfonos 726-3683 y 726-3633.



CALLE LOIZA # 1959, SANTURCE, P. R. 00914

## LISTA DE ANUNCIANTES

1. BELTONE ELECTRONICS	HEARING AIDS
2. BOEHRINGER INGELHEIM	TORECAN
3. BURROUGHS WELLCOME	CODEINE ANALGESICS, SEPTRA
4. CARNATION COMPANY	EVAPORATED MILK
5. CIBA PHARM.	VIOFORM - HC
6. EATON LAB.	FURACIN, MACRODANTIN
7. ROCHE LAB.	AZO-GANTANOL, BACTRIM, VALIUM
8. RORER INTERNATIONAL	MAALOX
9. SMITH, KLINE & FRENCH	DYAZIDE
10. SYNTEX LAB.	NEO-MULL-SOY
11. U. S. V. PHARM.	HYGROTON
12. UPJOHN COMPANY	MEDROL DOSEPAK





Continues to kill Staph. aureus  
and other burn wound invaders...

## **Furacin<sup>®</sup>** soluble dressing (nitrofurazone)

for dressing and re-dressing second- and third-degree burns

With the constant advent of new antibacterials, resistance patterns change...but today, as in 1947, Furacin (nitrofurazone) continues to be bactericidal against *Staph. aureus*, the most common burn wound invader, and one which frequently develops resistance to other antibacterials. Furacin is also bactericidal against most other bacteria commonly causing surface infection.

Furacin is painless and soothing on application, water-soluble, nonmacerating, and virtually nontoxic to tissue.

Furacin is available in tubes of 28 grams and 56 grams, and jars of 135 grams, 454 grams, and 5 pounds.

**Contains:** 0.2% Furocin (nitrofurazone). **Indications:** Adjunctive therapy for 2nd and 3rd degree burns when bacterial resistance to other agents is a real or potential problem. Skin grafting where bacterial contamination may cause graft rejection and/or donor site infections. **Contraindications:** Known prior sensitization to nitrofurazone. **Warnings:** Nitrofurazone has been shown to produce mammary tumors when fed at high doses to female Sprague-Dawley rats. The relevance of this to topical use in humans is unknown. **Safe use of nitrofurazone during pregnancy** has not been established. Use on women of child-bearing age is not recommended unless the therapeutic benefit outweighs the possible risk. **Precautions:** As with other topical antimicrobial agents, overgrowth of resistant organisms may occur. If this occurs, or if irritation, sensitization or superinfection develop, treatment with nitrofurazone should be discontinued and appropriate therapy instituted. **Adverse Reactions:** Furocin has not been significantly toxic in man by topical application. Sensitivity is low, with an overall incidence of 1.1 percent. Sensitivity reactions should be handled in a normal manner, except in the rare instance of severe contact dermatitis, when steroid administration may be indicated.



**EATON LABORATORIES**  
Norwich International  
410 Park Avenue, New York, N.Y. 10022, U.S.A.

# Septra® vs Nitrofurantoin

Each tablet contains:  
80 mg trimethoprim and 400 mg sulfamethoxazole

## A new clinical

### **Efficacy: A draw.**

By randomized assignment, 149 patients received two Septra tablets b.i.d. and 140 received one 100 mg capsule of nitrofurantoin macrocrystals q.i.d. for 14 days. Eight days after therapy ended, 94% of patients treated with Septra had a clear culture vs 90% of those treated with nitrofurantoin macrocrystals.<sup>1</sup>

### **Laboratory changes: A draw.**

There was no significant difference in the incidence of laboratory changes except in one instance; a significantly larger proportion of patients on nitrofurantoin macrocrystals had decreased lymphocyte counts than did patients on Septra.<sup>1</sup> The significance of this change is not known. (For further details see page three of this advertisement.)

### **Clinical side effects: Advantage, Septra.**

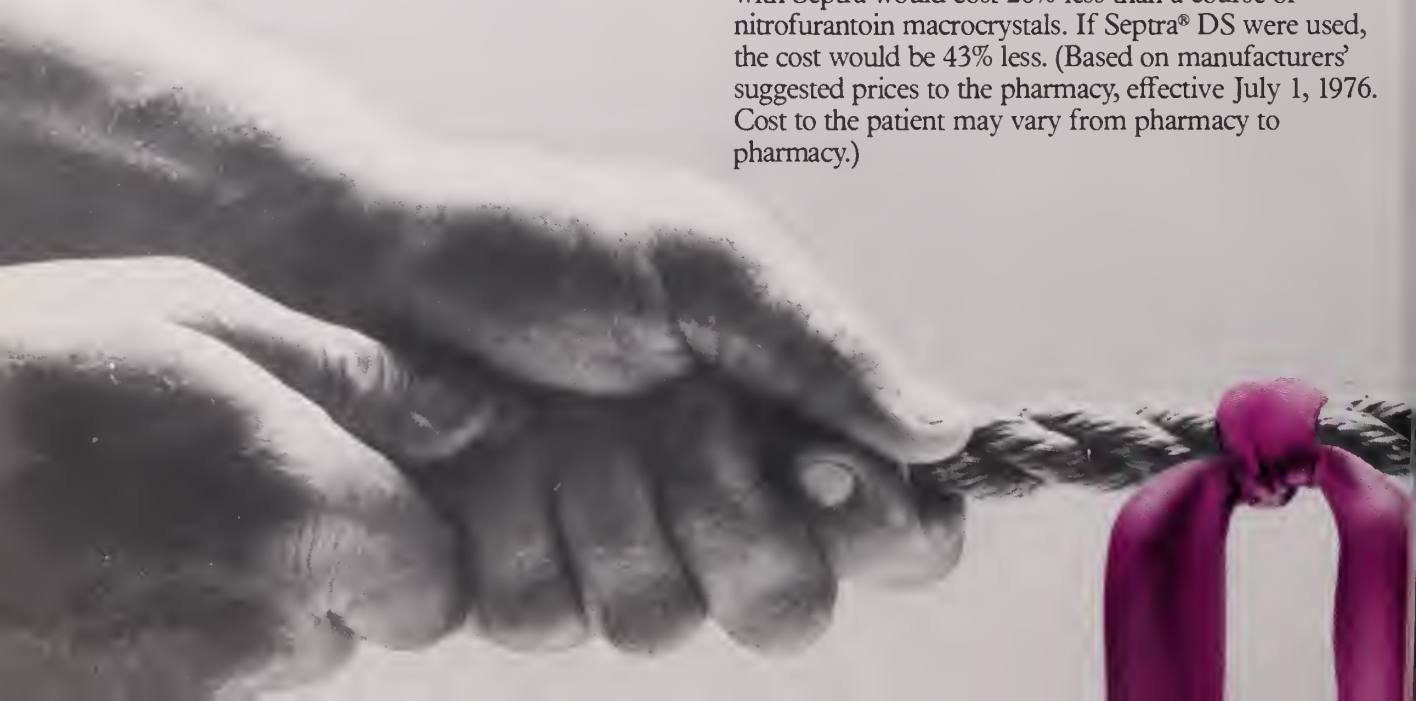
A significantly larger proportion of patients experienced side effects on nitrofurantoin macrocrystals (13%) than on Septra (6%).<sup>1</sup> (For further details, see chart on page three of this advertisement.)

### **Convenience: Advantage, Septra.**

To maintain effective antibacterial activity, Septra is taken just twice a day, while nitrofurantoin macrocrystals are taken four times daily. The Septra dosage schedule offers obvious advantages in terms of patient convenience and compliance.

### **Cost: Advantage, Septra.**

At the dosages used in this study, a course of therapy with Septra would cost 26% less than a course of nitrofurantoin macrocrystals. If Septra® DS were used, the cost would be 43% less. (Based on manufacturers' suggested prices to the pharmacy, effective July 1, 1976. Cost to the patient may vary from pharmacy to pharmacy.)





# rofurantoin

Macrocrystals

## confrontation

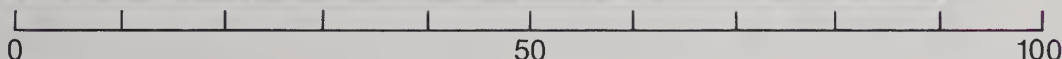
Results after 14-day course of therapy in 289 patients with recurrent urinary tract infections\*<sup>1</sup>

Septra

94%

Nitrofurantoin  
Macrocrystals

90%



% of patients with clear culture 8 days after therapy ended

\*Due to susceptible strains of *E. coli*, *Klebsiella*, *Enterobacter*, *Proteus mirabilis* and other *Proteus* species. Criterion for infection—100,000 or more organisms/ml urine. Criterion for "clear culture"—1,000 or fewer organisms/ml urine.

# Septra<sup>®</sup> DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

**Double Strength Tablets.**

**The most economical  
form of Septra.**

See next page for prescribing information.





# Septra<sup>®</sup> vs Nitrofurantoin

Each tablet contains:

80 mg trimethoprim and  
400 mg sulfamethoxazole

Macrocrystals

## Clinical side effects: Advantage, Septra.

Side effect	Frequency <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
nausea	3	16
vomiting	1	9
anorexia	1	4
abdominal pain	—	2
diarrhea	—	4
headache	2	—
dizziness	—	1
diaphoresis	1	—
pruritus	2	1
vaginitis	1	—
maculopapular rash	1	1
rash	—	2
urticaria	2	—
	14	40

**Note:** All patients who originally entered the study described on previous pages were included in the evaluation for clinical side effects (192 patients received Septra, 191 received nitrofurantoin macrocrystals). Some patients experienced more than one side effect. See **Adverse Reactions** section below for other reactions that may be encountered.

## Laboratory changes: A draw.

Type of change	Drug administered	
	No. patients with change/total patients tested <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
RBC ↓	14/141	14/141
Hemoglobin ↓	27/188	36/183
WBC ↑	3/188	3/183
" ↓	6/188	7/183
Bands ↑	3/183	3/176
" ↓	26/183	20/176
Hematocrit ↓	34/188	27/183
SGOT ↑	5/176	4/167
Basophils ↑	14/179	16/171
Neutrophils ↑	27/188	25/182
" ↓	3/188	6/182
Lymphocytes ↑	15/188	18/182
" ↓	11/188	21/182
Eosinophils ↑	14/179	8/177
Monocytes ↑	10/188	11/180
" ↓	23/188	23/180
Specific gravity ↑	1/187	—
" " ↓	—	1/177
Casts ↑	6/186	5/182
WBC/HPF ↑	9/190	13/185
RBC/HBF ↑	12/190	12/185
Bacteria ↑	9/189	11/183
" ↓	30/189	32/183
Crystals ↑	9/185	9/181

**Note:** Certain patients were not tested for some of the laboratory values listed above. Therefore, the chart specifies the total number of patients who completed the prescribed series of tests for each individual laboratory measurement.

**Indications:** Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37: 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. At present, data are insufficient to recommend use in infants and children under 12.

**Precautions:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria,

serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1 DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

**Supplied:** Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

**Reference:** 1. Data on file, Medical Department, Burroughs Wellcome Co.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

## To relieve nausea and vomiting associated with

- postoperative recovery
- radiation therapy
- chemotherapy
- acute situations

(Contraindicated in pregnancy, severe CNS depression, comatose states and in patients who have demonstrated a hypersensitivity to phenothiazines.)

## Three dosage forms with the same 10 mg dosage strength:

**Tablets**—10 mg (thiethylperazine maleate, NF)



**Suppositories**—10 mg (thiethylperazine maleate, NF)



**Injection**—10 mg/2cc ampul (thiethylperazine maleate, NF) for IM use only.



# Torecan<sup>®</sup>

(thiethylperazine)

Still available in  
Puerto Rico



**Boehringer Ingelheim**

Boehringer Ingelheim Ltd.  
Elmsford, New York 10523

**Torecan<sup>®</sup>** (thiethylperazine)

Tablets, Suppositories and Injection

**Contraindications:** Severe CNS depression, comatose states, and in patients who have demonstrated a hypersensitivity to phenothiazines (e.g., blood dyscrasias, jaundice). Because severe hypotension has been reported after the intravenous administration of phenothiazines, this route of administration is contraindicated. The drug is contraindicated in pregnancy.

**Warnings:** Phenothiazines are capable of potentiating CNS depressants as well as atropine and phosphorous insecticides. The drug may impair mental and/or physical ability required in the performance of potentially hazardous tasks such as driving a car or operating machinery. *Postoperative Nausea and Vomiting:* When used to control postoperative nausea and vomiting in patients undergoing elective surgical procedures, restlessness and postoperative CNS depression during anesthesia recovery may occur. Possible postoperative complications of a severe degree of any of the known reactions of this class of drug must be considered. Postural hypotension may occur after an initial injection, rarely with the tablet or suppository. Do not use with epinephrine in the treatment of drug-induced hypotension as phenothiazines may induce a reversed epinephrine effect. The most suitable vasoconstrictor agents are levaterenol and phenylephrine. The use of Torecan has not been studied following intracardiac and intracranial surgery. Not recommended for use in children under 12 years of age, or in nursing mothers since safety and efficacy have not been established.

**Precautions:** Convulsions and abnormal movements such as extrapyramidal symptoms have occurred. The varied extrapyramidal symptom complex is more likely to occur in young adults and children. Extrapyramidal effects must be treated by reduction of dosage or cessation of medication. For treatment of nausea and/or vomiting associated with anesthesia and surgery, the drug should be administered by deep intramuscular injection at or shortly before the termination of anesthesia.

**Adverse Reactions:** CNS: convulsions, extrapyramidal symptoms such as dystonia, torticollis, oculogyric crisis, akathisia and gait disturbances, occasional cases of dizziness, headache, fever and restlessness have been reported. Drowsiness may occur initially on injection but is usually alleviated by a reduction in dosage. Dryness of the mouth and nose, blurred vision, tinnitus, sialorrhea and altered gustatory sensation. Peripheral edema of the arms, hands and face. Cholestatic jaundice; cerebral vascular spasm and trigeminal neuralgia have been reported occasionally. The following have occurred with phenothiazine derivatives and should be considered: agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia, pancytopenia, eosinophilia, leukocytosis, miosis, obstipation, anorexia, paralytic ileus; erythema, exfoliative dermatitis and contact dermatitis; jaundice, biliary stasis. Hypotension, rarely leading to cardiac arrest; ECG changes. Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonos, oculogyric crises, tremor, muscular rigidity, akinesia, some of which have persisted for several months or years especially in patients of advanced age with brain damage. Menstrual irregularities, altered libido, gynecomastia, weight gain, false positive pregnancy tests. Urinary retention, incontinence; fever, laryngeal edema and angioneurotic edema, asthma. Hyperpyrexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. ECG changes. While there is no evidence that ECG changes are in any way precursors of any significant disturbance of cardiac rhythm, sudden and unexpected deaths apparently due to cardiac arrest have been reported in a few instances in hospitalized psychotic patients previously showing characteristic ECG changes. A peculiar skin-eye syndrome, which is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea, has also been recognized as a side effect following long-term treatment. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported.

**Drug Interactions:** Phenothiazines are capable of potentiating CNS depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorous insecticides. The drug may induce a reversed epinephrine effect on occasion.

For complete details, please see full prescribing information.



**anti-  
inflammatory**

**antifungal**

**antipruriti**

**antibacterial**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform® Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; lichenoid eczema and chronic eczematoid otitis externa; acne vulgaris; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Use in Pregnancy

Though topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain. If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression. May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

C75-38 Rev. 7/75

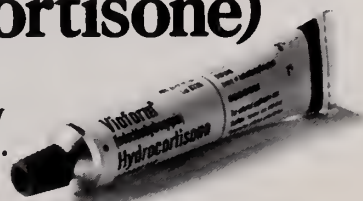
Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/7853 17

# Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A



**We've been delivering for  
four generations--and still cost less.**

Carnation Evaporated Milk formulas have been raising strong, healthy babies since 1899—delivering the good, sound, natural nutrition newborns and infants thrive on. You see, Carnation Evaporated Milk has naturally occurring protein with all other

nutrients intact. You indicate vitamins, iron and carbohydrates to meet each baby's needs.

Importantly, a whole formula made with Carnation Evaporated Milk still costs new mothers less than any other. Carnation Evaporated Milk...for four generations. The babies under your care will thrive on it, too.



**FREE!** Send for sample copies of these informative patient oriented booklets: "Preparing Your Baby's Formula," "You and Your Contented Baby"; Mail to: Carnation Company, GPO Box 682, San Juan, Puerto Rico, 00936.

Name \_\_\_\_\_  
Address \_\_\_\_\_  
City \_\_\_\_\_  
State \_\_\_\_\_ Zip \_\_\_\_\_

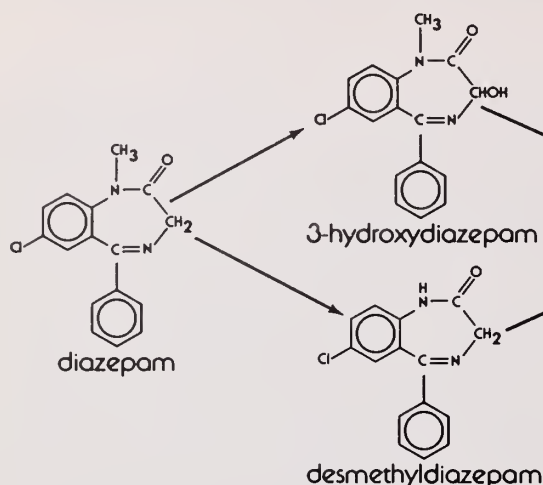
Proximate analysis (per 100g): Moisture 73.7g;  
Fat 7.9g; Protein 7.0g; Ash 1.5g; Carbohydrate 9.9g;  
Calories 138; Vitamin A 320 IU; Vitamin D 79 IU.  
CARNATION® EVAPORATED MILK, CARNATION COMPANY  
LOS ANGELES, CA 90036.







# A pharmacokinetic character all its own



**Valium (diazepam) is a benzodiazepine with a distinctive pharmacokinetic profile**

The pharmacokinetic profile of Valium is one of the characteristics that sets it apart from other benzodiazepines. Consider, in particular, the metabolic pathway of Valium. The three major metabolites of Valium exhibit significant pharmacologic activity—and so, of course, does the parent substance—diazepam itself. All combine to produce the characteristic clinical response seen with Valium. The response you have come to know, to want and to trust.

Pharmacokinetic studies also demonstrate that Valium has a pattern of absorption, distribution, metabolism and elimination that is reliable and consistent. And, although the pharmacokinetics of a drug cannot, at present, be specifically related to its clinical effects, it is clearly a factor that distinguishes one product from another by providing important insights into how each moves through the patient's body.

## Valium® (diazepam) <sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:**

Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma;

may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients.

Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

# "Mr. Chairman, Members of the Committee, I am Dr. Holden... Dr. Palmer ... Dr. Beddingfield ... Dr...."

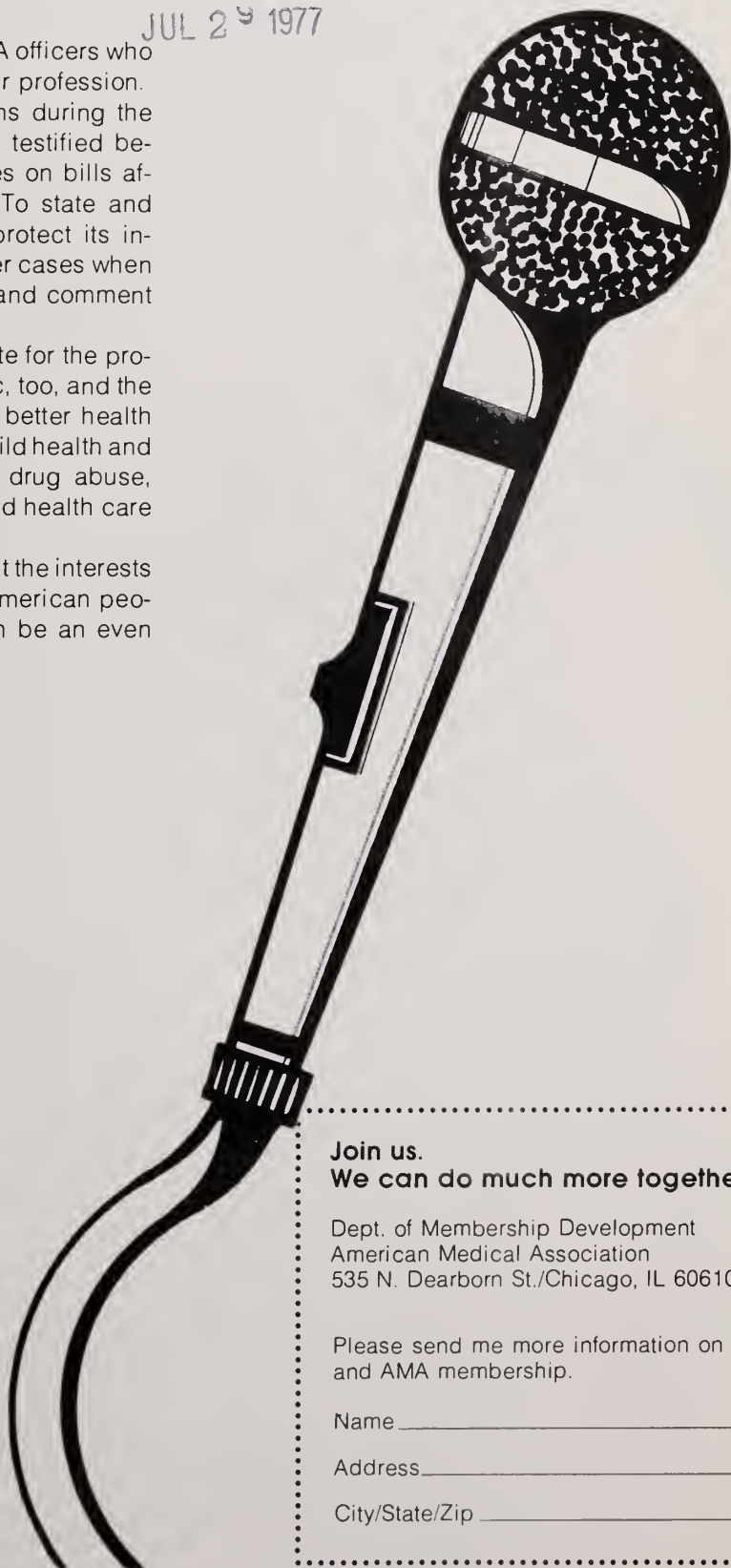
JUL 29 1977

These were but a few of the many AMA officers who have gone to the Hill to represent our profession.

On more than two dozen occasions during the 94th Congress, AMA representatives testified before Congressional health committees on bills affecting the delivery of health care. To state and explain our profession's views. To protect its interests. In addition, there were 72 other cases when the AMA submitted written analysis and comment on legislation.

But the AMA isn't solely an advocate for the profession. It's an advocate for the public, too, and the passage of legislation for more and better health care. Legislation such as maternal, child health and crippled children services. Alcohol, drug abuse, and mental health programs. Improved health care for American Indians.

The AMA goes to the Hill to represent the interests of the American physician and the American people. With your support, the AMA can be an even more effective spokesman.



**Join us.  
We can do much more together.**

Dept. of Membership Development  
American Medical Association  
535 N. Dearborn St./Chicago, IL 60610

Please send me more information on the AMA  
and AMA membership.

Name \_\_\_\_\_

Address \_\_\_\_\_

City/State/Zip \_\_\_\_\_

**anti-  
inflammatory**

**antifungal**

**antipruritic**

**antibacterial**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform® Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce. C75-38 Rev. 7/75

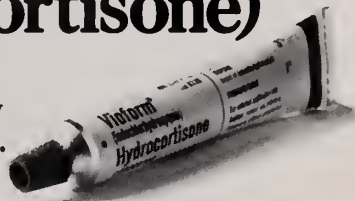
Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/7853 17

# Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

## ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial

Fundado en 1903

Volumen 69

Junio 1977

Número 6

## JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bermúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

## Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

## Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

## Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Evaluation of Medical Education: As Developed in The "Curso de Actualización Médica" .....	179
<i>Egidio S. Colón Rivera, MD, José E. Sifontes MD and Donald W. Keillor, MA</i>	
El Consorcio de Educación Médica del Oeste, Su Historia .....	188
<i>José Ramírez Rivera, MD, FACP</i>	
Cómo se Llegó a Ejercer la Medicina en Puerto Rico: 1976 .....	191
<i>José Ramírez Rivera, MD, FACP</i>	
Dígallo en Español or "Say It in English" .....	199
<i>José Ramírez Rivera, MD, FACP and Braulio Quintero, MD</i>	
Pólipos de la Uretra Posterior.....	206
<i>Juan R. Iturregui Pagán, MD y Roberto F. Fortuño, MD</i>	
Editorial- La Escuela de Medicina ante la Educación Médica Continuada.....	211
<i>Carlos E. Girod, MD</i>	
Book Review: Text Book of Black Related Diseases .....	213
<i>Alain Louis-Gustave, Docteur</i>	
Noticias .....	214

PORTADA - Caleta Las Monjas  
(Viejo San Juan)  
Cortesía: Dr. Rafael E. Ramirez

## EVALUATION OF MEDICAL EDUCATION: As Developed in The "Curso de Actualización Médica"

Egidio S. Colón Rivera, MD, José E. Sifontes, MD and Donald W. Keillor, MA

In Puerto Rico, at the present time, there are two areas in the field of medical education which are growing and becoming increasingly more important. The first area is that of Graduate Medical Education. This term is being used mainly to include internship and residency training programs. The second area is that of Continuing Medical Education for practicing physicians. This area includes the courses which are given for up-dating physicians.

In the area of Graduate Medical Education we have seen in the last ten years, and even more significantly in the last five years, an increase in the number of hospitals (government, non-profit and proprietary) which have initiated instructional programs for interns and residents. This has been due to many factors: an increase in the pool of candidates, the development of new hospital facilities such as the Mayagüez and the Caguas regional hospitals, and the "advantages" which these programs bring.

In the area of Continuing Medical Education, the change has occurred mostly in the past five years. This has been due mainly to the efforts of the School of Medicine of Puerto Rico,

the Puerto Rico Medical Association, the Puerto Rico Regional Medical Programs and the various health associations which sponsor programs as part of their activities (Heart, Lung, Cancer and others). The "Curso de Actualización Médica" at the School of Medicine and the Fifth Pathway Program at the Mayagüez Medical Center are two examples of the above. Plans for the future, which are now being developed, should result in a marked increase in continuing education opportunities for the physician. This is specially true at the School of Medicine. Of course, this has been in response to the well known, and proven need, of all physicians to keep up with new knowledge and skills which increase more rapidly each year.

The purpose of this communication is to emphasize the importance of proper evaluation for the validation and improvement of medical education programs, to review briefly the modern methods of evaluation and to present an example of their application.

### The Problem

As efforts in graduate and continuing medical education multiply, it becomes obvious that means or mechanisms are required to find out if objectives are being met and to what degree.

In the past, the general tendency had been to equate a "well-known physician" with a "good teacher" and though the principle still seems reasonable this does not necessarily mean that all "well known physicians" are also good

---

*From the Division of Continuing Medical Education, School of Medicine.*

*Originally presented at the Annual Meeting of Puerto Rico Medical Association, on November 1972, and subsequently updated and revised.*

*The study reported here was supported by Contract No. HSM - 110 - 69 - 405, sponsored by the National Center for Health Services Research and Development, U. S. Department of Health, Education and Welfare, and in part by the Department of Health of Puerto Rico.*



teachers. Teaching programs that appear, on paper, to be excellent, often turn out graduates who do not perform as well as expected.

Most of us have attended numerous conferences, work-shops, round-table discussions and other educational activities. Were they worthwhile? Did we learn anything? More important still, did they change our way of practicing medicine so that the patient benefited? *This is the critical question.*

### Evaluation in General

More and more those concerned with teaching programs, directors as well as instructors, become aware of the critical importance of adequate evaluation. Subjective evaluation, carried on mainly by the persons in charge of the programs, is increasingly noted to be inadequate. The lack of objectivity and the inherent bias of such evaluation makes it less desirable. Another approach is that of evaluating the increase in knowledge through the use of different types of examinations.

A more complete program of evaluation should evaluate the faculty, and the program, as well as the "student". Some of the methods which are presently being used are:

#### 1. *The Student:* (In the three main areas of learning)

##### 1. *Knowledge:*

Essay Examinations  
Oral Examinations  
Objective Examinations, mainly  
of the multiple choice type

##### 2. *Performance (Skills)*

Anecdotal Record  
Check Lists  
Rating Scales

##### 3. *Attitudes:*

The Interview  
The Log Diary  
Peer Rating  
Filmed Interview  
Problem Solving Tests

#### 2. *The Faculty:*

Questionnaires  
Videotapes  
Peer Review

#### 3. *The Program:*

Feed back from the above evaluating techniques  
Pre and Post-testing of the instructional activity  
Results from "Independent" testing agencies such as State Board Examinations, National Boards, Specialty Boards, etc.

These are some of the methods which can be utilized to evaluate the results of instructional activities, but it must be emphasized that proper evaluation must be preceded by the development of specific objectives, best stated in terms of observable terminal behavior. Unless the objectives of an instructional program are previously specified and known by all concerned, it is almost impossible to adequately evaluate program effectiveness.

One must determine, before a given program begins, how the student will be expected to perform when he meets at least the minimum requirements of stated objectives. If at a certain point in time the student cannot demonstrate that he meets acceptable levels of performance, then he continues learning until he can. When he finally demonstrates competency, he has successfully completed the program. On the basis that some students quite naturally take longer than others to reach certain levels, there is no penalty attached

as the time factor is not recorded. Learning psychologists call this, learning for mastery or simply, Mastery Learning.

Evaluation is undertaken to improve and perfect instructional programs so that minimum acceptable levels of performance conform to reasonable demands on the student and so that the time assigned for learning is adequate. Pre-testing students is done in order to determine their competencies before they are exposed to the instructional program. Re-evaluation of the competencies originally measured is done at the end of segments, or blocks of instruction, which relate to these competencies. This provides immediate information on whether or not the program is effective as it proceeds. It also provides basic and critical information essential for remedial action during the program as well as for future program modification. This is called *Formative Evaluation* as its purpose is to provide the essential data for the formation of a reasonable and effective instructional program.

At the conclusion of the program there is a *Summative Evaluation*. This is a comprehensive evaluation and provides the necessary information for the purpose of assigning grades or certifying competencies. The results of this terminal evaluation are used, along with the results of formative evaluation to provide important feedback information for assessing and improving the original instructional program.

An example of how this works will serve to define a process which we call "*The Chicago Loop*" (Fig. 1) and which consists of the sequence of objectives, learning experiences, and evaluation procedures with a feedback loop to the beginning of the sequence. It can be seen that evaluation serves the useful purpose of providing information for a revision of any, or all, elements in the sequence — including possible revision of the evaluation procedures themselves. A closed circle or "loop" indicates the interrelationships that exist among the



Figure 1

objectives, the learning experiences and the evaluation procedures. Other examples of the same process are presented in a slightly different format (Figs. 2 and 3).

#### An Example: The Evaluation of "Curso de Actualización Médica"

The "Curso de Actualización Médica" has been described elsewhere (1). In brief it was a course prepared by the faculty of the University of Puerto Rico School of Medicine for those Puerto Rican physicians who have graduated from foreign medical schools but not obtained passing grades on the Puerto Rico Board Examination or the ECFMG. Financing was provided initially through a contract with the National Center for Health Services Research and Development. Evaluation of this endeavor was divided into three areas: 1) evaluation of the course, 2) evaluation of the student's performance and 3) "On the job" evaluation. The Educational Testing Service of Princeton was awarded sub-contracts to assist us in the various phases of the evaluation.

## A BASIC TEACHING MODEL

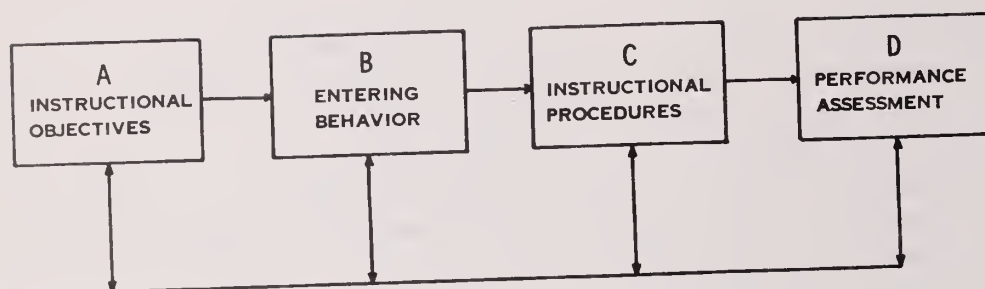


Figure 2

## EVALUATION PROCESS



Figure 3

1) *Evaluation of the Course:*

This was done by means of a questionnaire prepared by Dr. Jay Davis of the Educational Testing Service (2). One part of the questionnaire was filled out by the students at the completion of the entire work. The results were tabulated by the staff and discussed with the course Educational Consultant, representatives of the Educational Testing Service, and the Project Officer from Washington. In designating the

questionnaire every effort was made to avoid its becoming a "popularity poll". Many of the recommendations made by the students were implemented.

The course was also evaluated by the faculty, the coordinators of each area and the staff. This was done in more informal fashion at special meetings.

The faculty was evaluated by the students through the questionnaire and by the coordinators who were present during the teaching activities (peer-review). Also available on a voluntary basis was a faculty self-evaluation method utilizing videotapes made in the classroom and a rating scale for its interpretation (3).

2. *Evaluation of Student's Performance:*

- a) *Pre and Post-Testing:* The pretesting per area was done one or two weeks in advance of the scheduled classes so that it could be used as a "diagnostic examination" and the results be available to modify the instructional program so that obvious weaknesses could be remedied. The post-test per area was utilized as a "Teaching Examination". After the students had answered the examinations each question was discussed and any doubts



TABLE I  
A COMPARISON OF THE GAINS IN MEAN SCORES IN 12 AREAS OF MEDICAL  
KNOWLEDGE ACHIEVED BY THE PHYSICIANS IN THREE DIFFERENT COURSES \*

		COURSE I		COURSE II		COURSE III	
		Score	Percent	Score	Percent	Score	Percent
<i>Pre-Test</i>	<i>Anatomy</i>	14.31	35	13.85	34	15.02	37
	<i>Physiology</i>	13.25	33	14.00	35	15.46	38
	<i>Microbiology</i>	13.64	34	14.52	36	14.57	36
	<i>Biochemistry</i>	16.08	40	16.08	40	17.00	42
	<i>Pathology</i>	15.21	38	14.17	35	15.91	39
	<i>Surgery</i>	11.25	28	10.38	25	11.84	29
	<i>Obstetrics</i>	18.87	47	19.11	47	20.64	51
	<i>Gen. Medicine</i>	15.72	39	16.05	40	16.97	42
	<i>Community</i>						
	<i>Medicine</i>	15.70	39	15.44	38	15.31	38
	<i>Pediatrics</i>	17.66	44	17.05	42	18.11	45
	<i>Psychiatry</i>	15.78	39	15.47	38	15.37	38
<i>Post-Test</i>	<i>Anatomy</i>	17.54	44	15.81	39	17.60	44
	<i>Physiology</i>	18.60	46	17.75	44	19.82	49
	<i>Pharmacology</i>	19.86	49	18.71	46	20.40	51
	<i>Microbiology</i>	17.54	44	17.46	44	18.20	45
	<i>Biochemistry</i>	18.93	47	23.56	58	22.31	55
	<i>Pathology</i>	20.41	51	19.62	49	20.17	50
	<i>Surgery</i>	13.13	32	13.37	33	13.44	33
	<i>Obstetrics</i>	22.54	56	23.81	59	22.64	56
	<i>Gen. Medicine</i>	21.36	53	22.15	55	22.64	56
	<i>Community</i>						
	<i>Medicine</i>	19.10	47	20.09	50	18.73	47
	<i>Pediatrics</i>	21.52	53	21.90	54	25.04	62
	<i>Psychiatry</i>	17.63	44	18.75	46	18.33	45
<i>Pre-Test</i>	<i>Basic Sciences</i>	14.97	37	14.89	37	15.67	39
	<i>Clinical Sciences</i>	15.83	39	15.58	38	16.37	40
<i>Post-Test</i>	<i>Basic Sciences</i>	18.81	47	18.81	47	19.75	49
	<i>Clinical Sciences</i>	19.21	48	20.01	50	20.13	50
<i>Pre-Test</i>	<i>Grand Total</i>	15.40	38	15.23	38	16.02	40
<i>Post-Test</i>	<i>Grand Total</i>	19.01	47	19.41	48	19.94	49
	<i>Gain</i>	3.61	9.02	4.18	10.45	3.92	

\* - Based on the UPR Medical Knowledge Test administered before and after the course (each area had 40 questions equivalent to 40 points)

clarified.

- b) *"Mid-Course" Examinations:* One was given at the end of the first half of the course and another at the end of the second half of the course. These were dropped after the first course because they did not add any significant information and they were producing increased anxiety among the students.
- c) *Pre and Post-testing with the "UPR Medical Knowledge Test" and the Puerto Rico Licensure Examinations:* The UPR Medical knowledge test was prepared by members of the School of Medicine of the University of Puerto Rico. It is a multiple choice type of examination which is the subject of two very complete reports from the Educational Testing Service. The first report (4) is an analysis of the results in the first two courses that were given during 1970 and 1971. The analysis indicated that physicians in the two programs (1) were essentially equivalent prior to Course participation (2) showed significant but differential gain during the programs; and (3) performed somewhat better on subsequent Puerto Rico licensing examination than a group of foreign trained physicians from the general population. All indications, therefore, suggest the success of the course in increasing the medical knowledge of participants.

The second report (5) showed that many findings associated with Course I and II were substantiated by data gathered on Course III given in 1972. The course continued to attract and hold a substantial number of physicians. Moreover, these physicians also appeared to benefit from the course in terms of increased medical knowledge and greater probabi-

lity of medical licensure. The results in the pre and post-tests with the UPR Medical Knowledge Test are summarized in Table I and they show an average gain in each group of around ten (10) percent which is a *statistically significant gain*.

### 3) *"On the Job Evaluation"*

The original contract with HSM contained a provision for an evaluation of the post-training professional performance of graduates of the "Curso". Educational Testing Service was given a sub-contract to develop the methodology, procedure, and instruments. The decision was then made to conduct "On the - Job" evaluations after graduates had been working for approximately six (6) months. In addition, information was to be obtained on reaction follow-up combined with an audit of medical activities of these physicians and the attitudes of graduates regarding the "Curso" and its relevance to improved medical practice in different clinical settings. The planned evaluation was conducted in three ways:

#### a) *Interview:*

This covered the assignment, range of tasks, extent of community health involvement, future plans, nature of continuing medical contacts, reaction to the course program and its relation to the physician's situation.

#### b) *Observation of Premises:*

The interviewer, utilizing a guide, took notes concerning the physical setting, patient load, size of the center, number of staff and other related data.

#### c) *Questionnaire:*

TABLE II  
SUMMARY OF RESULTS IN THE STATE BOARD EXAMINATIONS  
FIRST "CURSO DE ACTUALIZACION MEDICA"

	U.S.A. Citizen	Foreign	Total	Percent
Enrolled First Course	21	29	50	
Completed First Course	21	26	47	
State Board Examination				
Outcome (Took Examination)	21	23	44	100
Passed	12	18	30	68
Failed	9	5	14	32
License: Regular *	12	0	12	27
Special ***	0	18	18	40
Sub-Total	12	18	30	68
Provisional **	4	--	4	9
Total :	16	18	34	77

SECOND "CURSO DE ACTUALIZACION MEDICA"

	U.S.A. Citizen	Foreign	Total	Percent
Enrolled Second Course	12	22	34	
Completed Second Course	11	21	32	
State Board Examination				
Outcome (Took Examination)	11	20	31	100
Passed	6	12	18	58
Failed	5	8	13	42
License: Regular *	6	--	6	19
Special ***	--	12	12	38
Sub-Total	6	12	18	58
Provisional **	5	--	5	16
Total :	11	12	23	74

THIRD "CURSO DE ACTUALIZACION MEDICA"

	U.S.A. Citizen	Foreign	Total	Percent
Enrolled Third Course	16	29	45	
Completed Third Course	16	29	45	
State Board Examination				
Outcome (Took Examination)	15	28	43	100
Passed	10	17	27	63
Failed	5	11	16	37
License: Regular *	10	1	11	26
Special ***	--	17	17	39
Sub-Total	10	18	28	65
Provisional	5	1	6	14
Total :	15	19	34	79

\* Represents Permanent License

\*\* License limited to one year (comparable to temporary license in U. S. A.)

\*\*\*License awarded to Foreign citizen only with practice limited to a government facility.



A questionnaire was used to obtain information about job satisfaction, difficulties encountered, and prevailing toward various aspects of the work settings (Fig. 3). It was completed by them at the time of the interview. (The intent was to get at the attitudes and reactions indirectly).

The results of this work are the subject of a very complete and detailed report from Educational Testing Service entitled "Follow Up of Course Graduates" by Dr. Roderick A. Ironside (6). The main facts brought out by this study are:

1. Most of the "Curso" graduates were in government service. Some were in District Hospitals, but most were in local Health Centers.
2. About seventy five percent (75 %) expected and wanted to continue in their government positions.
3. Graduates found the course of great benefit in their practice.
4. Most had constructive suggestions for revision of certain aspects of the Course. (These were taken into consideration and changes were implemented to improve the Course).

### Results.

The graduates of all three courses given showed a great deal of interest in the instruction they received. There is little doubt that being able to pass the State Board Examination was a *very strong motivational factor*.

The critical question here is, "How well did course graduates do on the State Board Examinations?" The complexities of licensing in Puerto Rico do not allow for a single answer to this question, therefore the results must be

based upon the different types of licenses which were extended by the State Board on the basis of results on different parts of the examination. This information is presented in Tabular form in Table II.

After the first course, twelve (12). U. S. citizens received a Regular License, and eighteen (18) obtained a Special License. This resulted in a total of thirty (30) physicians who obtained either a Regular or a Special License to practice. These physicians comprised sixty eight (68) percent of the group. An additional, four (4) physicians were granted a Provisional License. In the final analysis thirty four (34) physicians or seventy-seven (77) percent were granted a license to practice medicine.

After the second course six (6) U. S. citizens obtained a Special License. This made up a total of eighteen (18) physicians who obtained either a Regular or a Special License. They comprised fifty eight (58) percent of the group. In addition, five (5) more were granted a Provisional License. In all, a total of twenty three (23) physicians or seventy four (74) percent of those who took the examinations obtained a license.

After the third course ten (10) U. S. citizens and one (1) foreign obtained a Regular License. Five (5) U. S. citizens and one (1) foreign citizen obtained a Provisional License. Seventeen (17) foreign physicians obtained a Special License. This made up a total of twenty eight (28) physicians, sixty five (65) percent, who obtained either a Regular or a Special License to practice. In addition to these, six (6) were granted a Provisional License. All together thirty four (34) physicians or seventy nine (79) percent obtained a license to practice.

A second important question concerns the professional activities of "Curso" graduates. Up to the present time most have been assigned to areas of critical primary care health needs, some are in directive positions and some are working as specialists. A few have continued graduate training in a residency program. The impact of the course on the level of the *actual*

*practice of medicine* is the most difficult task to measure. Some work was done in developing adequate criteria and the development process was initiated at a workshop which took place at the Hotel Barranquitas on December, 1970; but this work was beyond the scope of the approved grant and could not be finished (7).

The above results must be analyzed taking into consideration that the selected candidates had already failed the Puerto Rico Licensing examination at least once, in many instances several times. This type of selection meant that our course would be trying to help physicians with definite and sometimes marked deficiencies. In addition to this the average age was around fifty (50) years which means that their potential for learning was diminished. Another added difficulty, and a very real one, was that in addition to acquiring new knowledge, graduates also had to forget previously acquired knowledge which had become obsolete. In some cases this prior knowledge was even potentially dangerous in the delivery health care.

Anxiety levels were also an inhibiting factor. In many instances it was too high and actually interfered with the learning process. Financial difficulties, absence from their families with schoolage children, with limited income, all these problems and many others had to be taken into consideration in trying to diminish their anxiety level.

### Conclusions

Evaluation of instruction is critical in determining what has been accomplished in a

given course. There are many ways in which this can be carried out, but a complete program should provide for the evaluation of the faculty and the content effectiveness of the course as well as of student learning. The evaluation of the "Curso de Actualización Médica" was based on the course, student learning and "On the Job" performance. This provided essential information for instituting the changes needed for improving subsequent courses.

When one considers the handicaps of the trainees and the actual number of physicians who received a license and who were then available for service especially in areas of critical need, it can be stated that final results met our original expectations.

### References

1. Colón, E. S., Sifontes, J. E.: Post Graduate Medicine in Puerto Rico (A Refresher Course). BoL Asoc. Med. P. Rico 64: 211-217, 1972.
2. Final Report, Contract HSM 110-69-405, Appendix - H: "Questionnaire for Evaluation of the Course", J. A. Davis.
3. Final Report, Contract HSM 110-69-405, Appendix - I: "Program for Self-Evaluation of Teaching: Videotapes", E. S. Colón.
4. Final Report, Contract HSM 110-69-405, Appendix - J: "Impact of the Curso de Perfeccionamiento: An Audit of the Effectiveness of the Physicians Retraining Program at the University of Puerto Rico. Final Report for Cursos 1 and 2", G. J. Burkheimer and J. A. Davis.
5. Final Report, Contract 110-69-405, Appendix K: "The Effectiveness of the Physician Retraining Program at the University of Puerto Rico - Final Report for Curso III", D. E. Powers.
6. Final Report, Contract 110-69-405, Appendix L: "Follow up of curso Graduates" R. A. Ironside.
7. Final Report, Contract 110-69-405, Appendix N: "Initial Development of Criteria of an Assessing Quality of Medical Care", R. A. Ironside.

# EL CONSORCIO DE EDUCACION MEDICA DEL OESTE

## SU HISTORIA

José Ramírez Rivera, MD, FACP

Consortio, dice el Pequeño Larousse que yace en mi escritorio, es la unión de los que viven juntos. Consortes son personas u entidades que comparten su suerte o desgracia. Celebramos esta mañana, señoras y señores, la iniciación formal de un Consortio, un enlace entre la Facultad de Medicina de la Escuela de Medicina de Puerto Rico y la Facultad de Medicina del Centro Médico de Mayagüez.

Los propósitos de esta unión han sido ampliamente difundidos. Son propósitos nobles y poderosos: una preparación más real para el estudiante de medicina puertorriqueño, una educación actualizada y vigorosa para los internos y residentes en tres hospitales regionales y un ambiente de superación para los médicos en la práctica privada o gubernamental en la Región Central, la Región del Sur y la Región Oeste de Puerto Rico.

Pero confesamos que en la Región Oeste celebramos con doble regocijo. Celebramos y hacemos público hoy un antiguo matrimonio escondido, contrato firmado agosto 8, 1974 por el actual Secretario de Salud y el entonces Rector del Recinto de Ciencias Médicas, Adán Nigaglioni, y que en parte decía así:

“Este contrato se lleva a cabo en interés de la educación médica, tanto por parte del Recinto como por parte del Departamento de Salud para que estudiantes de medicina conozcan otros talleres de trabajo que no sean únicamente los del Centro Médico de Puerto Rico en Río Piedras y se sientan motivados en otras comunidades trayendo como consecuencia una mejor distribución de médicos en Puerto Rico.

Este contrato está sujeto a las siguientes:

### *Cláusulas y Condiciones*

*Primero:* El Recinto reconoce al Centro Médico de Mayagüez y en específico a su hospital, como taller clínico acreditado y afiliado a su Escuela de Medicina.

*Segundo:* El Recinto utilizará para programas de adiestramiento y educación el Centro Médico de Mayagüez y cualquier otro hospital o instalación clínica del Departamento de Salud que en el futuro las partes, de común acuerdo, establezcan.”

Ese matrimonio secreto a que aludimos legitimizó un concubinato de tres años entre el Recinto de Ciencias Médicas y el Hospital Base en la Sultana del Oeste, concubinato intelectual y práctico que surgió de una manera

---

*Del Departamento de Educación Médica e Investigaciones Clínicas, Región Oeste de Salud.*

*Edición de charla presentada en la inauguración del Consortio Educativo de Medicina de la Región Oeste el 27 de mayo de 1976.*



natural y saludable para el servicio de una comunidad.

¿Quién era esa comunidad? Los estudiantes de medicina ignorados. Los jóvenes puertorriqueños que deambulaban por las ciudades de Madrid, Montpellier, Barcelona, Cali, Guadalajara o Santo Domingo, en búsqueda de educación médica. Estudiantes de medicina que llegaban angustiados a su patria al margen de la estructura educacional establecida, cargando cartas y pergaminos que indicaban haber más o menos terminado la carrera de medicina. La comunidad la comprendían médicos orientados a continuar su desarrollo en ambientes no pedagógicos donde se les indicaba como una imprescindible pero difícil meta obtener su licencia profesional (1).

La relación orgánica con la escuela de medicina se inició cuando el Centro Médico de Mayagüez, con bendición Universitaria, fue uno de los diez primeros hospitales en la Nación Americana a ofrecer un último año de medicina clínica a cualificados estudiantes norteamericanos y puertorriqueños de universidades extranjeras, la importante quinta trayectoria. La relación adquirió una dimensión amplia cuando Mayagüez desarrolló un curso teórico-práctico paralelo a la quinta trayectoria para médicos sin credenciales para hacer un internado reconocido por la Asociación Médica Americana, curso que el *Tribunal Examinador de Médicos* estuvo dispuesto a reconocer como internado (2). El juego académico mayaguezano desplegó virtuosidad y preocupaciones universitarias al originar la Oficina de Educación Médica del Centro Médico de Mayagüez una solicitud federal por 1.2 millones de dólares a través de cinco años para pagar profesores visitantes y comprar materiales educativos para estos nuevos cursos. Viendo el mérito de esta propuesta, el Departamento de Salud concedió 10 becas post-graduadas de \$400 mensuales para que el médico recién llegado y sin experiencia clínica se desviara de la trayectoria usual

y sub-óptima del "internado jíbaro" \* desarrollando mejor sus destrezas en un taller educativo apropiado. Mayagüez demostró su firme propósito de ayudar a encauzar al estudiante de medicina olvidado al enviar nuestra oficina de Educación Médica cartas de orientación a todos los estudiantes de medicina en el extranjero becados por el pueblo de Puerto Rico (3).

El enlace académico entre el Recinto de Ciencias Médicas y el Centro Médico de Mayagüez terminó trágicamente, (diríamos hoy felizmente), en febrero de 1975. La crisis fiscal del pueblo de Puerto Rico forzó al Departamento de Salud a cancelar el contrato que prometía proveer mínimos pero esenciales recursos educativos para el desarrollo del Centro Médico de Mayagüez como una institución de enseñanza. Terminó cuando ya había evolucionado el concepto de la necesidad imperiosa que la Escuela de Medicina de Puerto Rico extendiera su organización y sus capacidades de enseñanza a todas las regiones de la Isla. Trató de terminar cuando la escuela de medicina de Puerto Rico, alentada en parte por el exitoso experimento Mayaguezano, ya había aceptado trascender la enclave capitalina para volcar su nutritivo caudal educacional a todos los médicos de Puerto Rico no importa cual fuera la escuela de la cual ellos fueran diplomados.

En febrero de 1975 negar que se extendiera la fuerza educativa de la escuela de medicina a los Hospitales Regionales de Puerto Rico fue conceptualmente inaceptable. La cancelación forzosa del tenue enlace académico entre el Recinto de Ciencias Médicas y el Centro Médico de Mayagüez desencadenó un movimiento histórico para la medicina puertorriqueña a la quinta hora de la tarde del primer jueves de marzo de 1975.

La historia sigue así: ante la imposibilidad de fortalecer y desarrollar los anémicos talleres

---

\* "Se prohíbe terminantemente al interno usar el microscopio", rezaba una cartulina mugrienta en la puerta del laboratorio de un hospital regional.

educativos en los Hospitales Regionales sin dinero, el Secretario de Salud, Dr. José A. Alvarez de Choudens, y el Decano de Medicina, Dr. Carlos Girod, se dirigieron a los líderes de la Cámara y el Senado por vía telefónica. Se concertaron citas urgentes para el martes y jueves de la semana siguiente con los ojos puestos en el fin inminente de la sesión legislativa. En estas citas se sembraron las fecundas semillas para la resolución conjunta de la legislatura que proveyeron \$400,000 que han hecho posible la apertura del consorcio educativo médico puertorriqueño. Y lo digo en singular pues debe ser solo uno: Consorcio Educativo de Educación Médica: Región Central, Región Sur, Región Oeste, REGION PUERTO RICO.

No queremos que opaque el hecho de abrir nuestras aulas ampliamente a estudiantes de medicina de tercero y cuarto año de la Universidad de Puerto Rico que el Centro Médico de Mayagüez es una escuela post-graduada con su propia estirpe desde su inicio.

En el próximo año educaremos aquí a 20 internos y a 50 o 60 residentes en diferentes especialidades y tenemos cabida como hemos tenido desde 1971, para 16 estudiantes puertorriqueños de Guadalajara, Santo Domingo, Colombia o España que necesiten ciertas electivas o un último año de experiencias clínicas antes de empezar el internado.

Quiero darle las gracias a la Facultad Médica del Centro Médico de Mayagüez a la Escuela de Medicina y al Gobierno de Puerto Rico por permitirme colaborar en una labor tan encomiable para la salud y la sociedad puertorriqueña.

### Referencias

1. *Ramírez Rivera, José*: El Camino Real (Editorial), Bol Asoc. Médica de Puerto Rico 65: 199, 1973.
2. *Jiménez Méndez, Alejandro*: ¿Por qué un Curso Teórico Práctico para Graduados del Extranjero? 65: 192, 1973.
3. *Ramírez Rivera, José*: Cómo se llega a practicar la Medicina en Puerto Rico: 1974, Buhití 5: 14, 1973.

## COMO SE LLEGA A EJERCER LA MEDICINA EN PUERTO RICO: 1976

José Ramírez Rivera, MD, FACP

**Summary:** We have gathered the information applicable to students of Medicine recently graduated about the law and the modifications of the law that regulates the practice of medicine in Puerto Rico. Contemporary information about the examination and how to obtain certification by the Educational Council of Medical Foreign Graduates has been detailed. The educational alternatives of the theoretical-practical course versus an internship not recognized by the American Medical Association for the graduates of foreign medical schools has been discussed. We favored the theoretical-practical course as a clinical experience which will better prepare a candidate for the "ECFMG" or the second and third part of the examination of the Board of Medical Examiners.

The five pathways that will allow Puerto Ricans studying in a foreign medical school to become eligible to continue their undergraduate or postgraduate in medical training in a system recognized by the AMA are presented. The fifth pathway is discussed emphasizing that students of schools that require a year of internship and/or a period of social service before receiving the degree of doctor of medicine should follow this pathway or should obtain their degree. Gra-

duates from these schools which have had an unapproved internship in Puerto Rico and do not have their degree are not acceptable as interns or residents in hospitals recognized by the AMA for graduate training even though they have approved in its entirety the examination of the Board of Medical Examiners of Puerto Rico. Residencies in hospitals of the Commonwealth no longer count as social service. The hospitals authorized by the Board of Medical Examiners to offer internships and the number of vacancies available have been tabulated.

**Resumen:** Recopilamos la información, aplicable a estudiantes de Medicina recién graduados, de la ley que regula la práctica de Medicina en Puerto Rico con todas sus enmiendas. Expone-mos también información actualizada de cómo se obtiene el examen y el certificado del Consejo Educacional de Médicos Graduados (ECFMG). Favorecemos un curso teórico-práctico, pre-internado para mejorar preparar un candidato para el ECFMG o la segunda y tercera parte de la reválida de Puerto Rico.

Las cinco trayectorias que permiten a un puertorriqueño estudiando en una escuela extranjera hacerse elegible para continuar estudios de medicina o post-graduados dentro del sistema educacional reconocido por la Asociación Médica Americana son presentadas. La quinta trayectoria es discutida recalcando que los estudiantes de escuelas que requieren un año de servicio social y/o período de servicio público para ofrecer un título deben seguir esta trayectoria u obtener su título. Los egresados de estas escuelas que hayan hecho inter-

---

*Del Departamento de Educación Médica e Investigaciones Clínicas, Región Oeste de Salud, y el Consorcio Educativo de Medicina, Mayagüez, Puerto Rico.*

*Nueva Edición Narrativa de carta dirigida a los estudiantes de medicina en escuelas extranjeras becados por el pueblo de Puerto Rico el primero de junio de 1974.*

*Solicite separadas al: Centro Médico de Mayagüez, Mayagüez, Puerto Rico 00708.*



nados no reconocidos en Puerto Rico y que no hayan obtenido su título no son aceptables para internados o residencias en hospitales reconocidos por la Asociación Médica Americana para estudios postgraduados aún cuando hayan aprobado en su totalidad la reválida de Puerto Rico.

Residencias en hospitales del Estado Libre Asociado ya no cuentan como servicio público. Los hospitales autorizados para ofrecer internados por el Tribunal Examinador de Médicos y las plazas disponibles han sido tabuladas.

La Ley que regula la práctica de la Medicina en Puerto Rico fue aprobada el 22 de abril de 1931, pero desde entonces ha sido enmendada repetidas veces, la última, el 23 de julio de 1976 (1).

Poco después de regresar a la Isla en el 1970, el autor se percató de la extraordinaria desorientación del puertorriqueño estudiando Medicina en el extranjero con relación a trayectorias apropiadas que lo pudieran llevar a ejercer esta profesión en Puerto Rico. En el 1973 enviamos 12 páginas de orientación a 518 estudiantes de Medicina en escuelas extranjeras registradas en el Departamento de Instrucción como becados por el pueblo de Puerto Rico. La favorable acogida de esta carta nos estimuló a una segunda edición la cual, ya en forma narrativa, se publicó en Buhití con el fin de que sirviera a la vez como resumen informativo para el Claustro del Recinto de Ciencias Médicas (2).

Los cambios de ley efectivos en junio de 1976 han hecho necesario una actualización de esta orientación. Ya que el estudiante espera que el médico en la práctica de la medicina conozca cómo llegar a ejercer su profesión en nuestro país, nos ha parecido apropiado presentar estos datos en *El Boletín*.

### Licencia

Para ejercer libremente la Medicina en Puerto Rico, como médico generalista o especia-

lista, se necesita una LICENCIA PERMANENTE que expide el Tribunal Examinador de Médicos de Puerto Rico (1).

Antes de esta Licencia Permanente el Tribunal expide una LICENCIA PROVISIONAL que permite practicar medicina en una facilidad médica específica. Esta licencia puede usarse solamente mientras se hace el internado o residencia y se trabaja en el Servicio Público y es renovable anualmente por un período de tiempo que en general no excede de tres años.

Para obtener la LICENCIA PROVISIONAL del Tribunal se requiere:

- 1) Haber aprobado por lo menos la primera parte de la reválida o exámenes equivalentes (FLEX o "National Boards").
- 2) Presentar una carta de aceptación para Internado o Residencia de un hospital acreditado por el Tribunal para ese propósito.

Para obtener la LICENCIA PERMANENTE se requiere:

- 1) Ser mayor de edad y ciudadano de los Estados Unidos o haber residido con visa de permanencia en Puerto Rico por un mínimo de tres años.
- 2) Poseer un diploma, o un título de médico-cirujano o un certificado de haber completado satisfactoriamente todos los estudios académicos de la carrera de médico-cirujano, que haya sido expedido por alguna universidad cuyo curso de estudios esté aceptado y registrado por el Tribunal Examinador de Médicos de Puerto Rico.
- 3) Ser una persona de moral intachable.

Además de estos requisitos, obvios para todo médico, se exige:

- 4) Haber terminado un INTERNADO reconocido por el Tribunal.
- 5) Haber aprobado la REVALIDA que ofrece el Tribunal o su equivalente (FLEX o "National Boards" o la reválida de otro estado con quien

tengamos reciprocidad).

- 6) Haber trabajado un mínimo de un año en el Servicio Público de Puerto Rico. Este *requisito es adicional al requisito de internado y a cualquier período de residencia que el aspirante haya completado* (3).

La solicitud de la licencia provisional debe llegar al Tribunal por lo menos 30 días antes de empezar el adiestramiento, ya que sin licencia no se permite comenzar.

### Reválida

La Reválida es ofrecida por el Tribunal Examinador de Médicos de Puerto Rico por lo menos dos veces al año. Consiste de tres partes: la primera incluye las Ciencias Básicas: Anatomía e Histología, Fisiología e Higiene, Bacteriología, Anatomía Patológica, Farmacología, incluyendo Medicina Legal, Toxicología, Materia Médica y Terapéutica; la segunda incluye las materias clínicas: Obstetricia, Ginecología, Medicina, Cirugía, Medicina Tropical; la tercera es un examen práctico en un hospital de la isla designado por el Tribunal. Los exámenes son en español e inglés y de tipo moderno (selección múltiple). Para aprobarlos es necesario obtener una calificación no menor de 75 en cada parte. La solicitud se obtiene del:

Tribunal Examinador de Médicos de PR  
Apartado 3271  
San Juan, Puerto Rico 00904

Esta debe radicarse con no menos de un mes de antelación a la fecha de los exámenes.

Para solicitar la primera parte de la reválida se exige evidencia oficial de haber aprobado todos los cursos de Ciencias Básicas, una carta del Decano de la Universidad, el Certificado de Nacimiento y un certificado de buena conducta de la policía. Para solicitar la segunda y tercera o para tomar las tres partes de la reválida a la vez, se requiere evidencia oficial

de haber terminado los estudios de Medicina (diploma, título, certificado), una transcripción oficial de notas y un retrato, un comprobante de pago de \$30.00 y un sello de Rentas Internas de \$1.00 (Los documentos oficiales debidamente legalizados).

Con la primera parte de la reválida se puede hacer un internado *no reconocido* por la Asociación Médica Americana (AMA) y "el año" de Servicio Público. No se puede hacer un internado *reconocido* por la AMA ni se pueden hacer estudios de especialidad hasta aprobar la reválida completa o su equivalente.

A partir de la primera solicitud hay cinco oportunidades, cinco convocatorias consecutivas, para aprobar la reválida. Si se fracasa o no se acuden a las cinco convocatorias, se deberá repetir el internado o tomar un curso de actualización médica de seis meses que sea aceptado por el Tribunal.

Es prudente y recomendable prepararse para tomar la primera parte de la reválida al teminar los estudios de las Ciencias Básicas (los 2 o 3 primeros años de estudio). Es claramente beneficioso para el que estudia en el extranjero obtener un certificado legalizado de haber terminado los estudios antes de regresar al país, para poder solicitar las dos últimas partes de la reválida o el certificado del ECFMG sin tener que esperar angustiosamente por la llegada del título.

### Flex

Este es el examen de reválida de la Federación de Tribunales Examinadores Médicos de los Estados Unidos, Federación a la cual nuestro Tribunal pertenece. Tiene aceptación en los Estados Unidos y Puerto Rico. El examen se ofrece en diciembre y junio y cuesta \$68.00. Se recomienda tomar este examen en vez de la reválida local por ser éste expertamente redactado y de mayor aceptación para estudios postgraduados. Al momento el FLEX se ofrece solo en inglés y por ley no se puede exigir como examen de reválida. Se espera que en un futuro cercano



este examen, con sus preguntas redactadas en español y en inglés, será nuestro examen de reválida. La solicitud se obtiene del:

Tribunal Examinador de Médicos de PR  
Apartado 3271  
San Juan, Puerto Rico 00904

La solicitud debe radicarse por lo menos con 45 días de anticipación.

### ECFMG

El examen del Consejo Educacional para Médicos Graduados en el Extranjero, (ECFMG), mide conocimientos de medicina y del idioma inglés. El examen se ofrece dos veces al año (enero y julio) en varios centros de diversos países. Puede solicitarse y aprobarse aún antes de graduarse de médico. Su aprobación provee el modo más rápido de obtener un internado reconocido aquí o en los Estados Unidos. Se solicita el examen del:

Educational Council for Foreign Medical  
Graduates  
3624 Market Street  
Philadelphia, Penn. 19104

La solicitud debe devolverse, antes de la fecha límite publicada, acompañada de un giro bancario de \$75.00, tres fotografías recientes tamaño pasaporte estampadas con el sello notarial de la escuela y una fotocopia del diploma. Los documentos deben estar debidamente legalizados.

Los resultados de este examen son enviados directamente al examinado de 6-8 semanas después de haberlo tomado. Una vez aprobado éste, el ECFMG expide un certificado provisional de seis meses al recibir evidencia de que el estudiante ha terminado la carrera. El certificado permanente se expide después de recibir una copia del Título.

Este certificado capacita para hacer internado en cualquier estado de los Estados Unidos y Puerto Rico; muchos estados lo exigen para

estudiar una especialidad en ellos y muchas juntas de especialidad (ej.: la de Cirugía y Oftalmología) lo tienen como requisito ineludible para certificarse en esa especialidad.

Se recalca que éste es solo un examen de *entrada* a estudios post-graduados y que es necesario obtener *el certificado* para poder seguir una residencia o internado reconocido por la AMA. Hay que tomar la reválida o el FLEX para poder obtener una licencia permanente. Al presente se requiere *la primera parte de la reválida más el ECFMG* o la reválida completa para empezar el Internado *reconocido* en Puerto Rico.

### Internado

En Puerto Rico hay dos categorías de internados. Uno es *reconocido* por la Asociación Médica Americana (AMA) y por el Tribunal Examinador de Médicos de Puerto Rico; el otro es reconocido solamente por el Tribunal Examinador de Médicos de Puerto Rico. (*no reconocido por la AMA*).

El internado *reconocido* por la AMA tiene lugar en hospitales, que en general, están mejor preparados para la labor de iniciar al recién graduado en la práctica de la medicina, tanto por las facilidades físicas (edificio y equipo) como por el personal médico a cargo de instrucción y de la orientación. Este internado que puede ser *flexible* o *directo*, es frecuentemente, un requisito para ser admitido a estudiar una especialidad.

El internado *flexible* es un entrenamiento clínico en varios de los departamentos del hospital incluyendo, por lo general, Sala de Emergencia. Este entrenamiento provee una transición apropiada desde sistemas educativos que proveen poca experiencia clínica al nuestro y es un paso acertado en la preparación de un médico de familia.

El internado *directo* es conveniente para médicos ya decididos y orientados hacia una especialidad, usualmente se ofrece a personas que han tenido una orientación clínica com-



pleta en todas las fases de la medicina.

El internado *no reconocido*, en general, expone al recién egresado a experiencias para las cuales él no está preparado sin suficiente ni apropiada supervisión. Tiene más carácter de servicio que de educación. No provee acceso a residencias en hospitales reconocidos ni a la especialización. Legalmente, sin embargo, se considera como suficiente para hacer el servicio público y practicar medicina en Puerto Rico si se pasa la reválida completa. No recomendamos el internado no reconocido por sus deficiencias educativas (4). Recomendamos una experiencia formativa *pre-internado* en hospitales de enseñanza, (la quinta trayectoria, el curso teórico-práctico) que lleven a un desarrollo profesional sin trabas (vide infra) (5). No creemos que este internado no reconocido forma el profesional de salud que el país necesita. Creemos que no prepara médicos satisfechos con sus conocimientos y destrezas, capaces de mantenerse actualizados.

### La Quinta Trayectoria

Los egresados del extranjero *sin título* de Doctor en Medicina no pueden continuar sus experiencias post-graduadas en hospitales donde la instrucción es reconocida y escrutinizada por la AMA sin hacer la Quinta Trayectoria. Aún cuando pasen el ECFMG y la reválida completa, la Quinta Trayectoria es exigida y no es sustituible por un internado *no reconocido*. Ya que las diversas avenidas que llevan a una educación post-graduada sin trabas son fuentes continuas de confusión nos apresuramos a detallarlas.

Hay cinco trayectorias que permiten a un puertorriqueño que estudia en una escuela de medicina extranjera hacerse elegible para continuar sus estudios de Medicina o sus estudios postgraduados dentro del sistema educacional reconocido y aceptado por la Asociación Médica Americana (6).

*Primera Trayectoria:* Transfiriéndose a una escuela de medicina norteamericana al completar

el tercer año después de obtener una nota satisfactoria en el examen de la Junta Nacional de Examinadores Médicos (National Board of Medical Examiners). Sistema COTRANS — “Coordinated Transfer System.”

*Segunda Trayectoria:* Aprobando el ECFMG y la primera parte de la reválida.

*Tercera Trayectoria:* Obteniendo una licencia permanente y sin restricciones para practicar medicina, expedida por un estado o agencia norteamericana autorizada convalidable en Puerto Rico.

*Cuarta Trayectoria:* Obteniendo una licencia provisional como primer paso hacia una licencia permanente y sin restricciones en aquellos estados que otorgan la licencia permanente sin ningún examen adicional después de que el médico haya completado satisfactoriamente un internado o residencia. *Para ser elegible para esta trayectoria, el médico graduado del extranjero deberá haber terminado todos los requisitos educacionales que lo hacen elegibles para certificación por el ECFMG.* (Tiene que tener TITULO).

*Quinta Trayectoria:* Esta trayectoria es aplicable a estudiantes que hicieron sus estudios de pre-médica en un Colegio o Universidad norteamericana y que estudian medicina en una universidad extranjera que exige un internado y/o un período de Servicio Social para darle el título de médico. La Asociación Médica Americana acepta sustituir este internado y/o período de Servicio Social por un curso clínico de diez meses bajo el auspicio de una escuela de medicina norteamericana. Tras aprobar este curso al estudiante se le considera capacitado para continuar estudios post-graduados sin ningún examen adicional, como si se hubiera graduado de una escuela norteamericana. Este concepto está teniendo una amplia aceptación en los diversos estados de la Unión, aunque muchos de ellos exigen el ECFMG como requisito para expedir una licencia permanente.

Es requisito para ingresar a este curso haber aprobado el ECFMG, la primera parte del examen de la Junta Nacional de Examinadores (National Board of Medical Examiners), o un

## HOSPITALES AUTORIZADOS PARA OFRECER INTERNADO Y NUMERO DE PLAZAS DISPONIBLES

<i>Hospital</i>	<i>Plazas</i>	
	<i>1976</i>	<i>1977-78</i>
<i>Sub-Regional - Aguadilla</i>	<i>12</i>	<i>25</i>
<i>Distrito - Arecibo</i>	<i>20</i>	<i>30</i>
<i>Municipal - Arecibo</i>	<i>6</i>	<i>7</i>
<i>Regional - Bayamón</i>	<i>22</i>	<i>36</i>
<i>SUB-REGIONAL - Caguas</i>	<i>22</i>	<i>33</i>
<i>Regional - Fajardo</i>	<i>22</i>	<i>30</i>
<i>AUXILIO MUTUO - Hato Rey</i>	<i>---</i>	<i>10</i>
<i>CENTRO MEDICO DE MAYAGUEZ</i>	<i>22</i>	<i>32</i>
<i>Municipal de Mayagüez</i>	<i>6</i>	<i>6</i>
<i>DISTRITO - Ponce</i>	<i>20</i>	<i>40</i>
<i>UNIVERSITARIO - Río Piedras</i>	<i>36</i>	<i>50</i>
<i>MUNICIPAL - San Juan</i>	<i>36</i>	<i>38</i>
<i>VETERANOS - San Juan (Federal)</i>	<i>14</i>	<i>30</i>
<i>La Concepción - San Germán</i>	<i>8</i>	<i>8</i>
<i>PRESBITERIANO - Santurce</i>	<i>---</i>	<i>8</i>
<i>San Carlos - Santurce</i>	<i>6</i>	<i>6</i>
<i>EL MAESTRO - Hato Rey</i>	<i>---</i>	<i>6 o 7 *</i>
<i>Area de Guayama</i>	<i>---</i>	<i>10</i>
<i>Area de Humacao</i>	<i>---</i>	<i>12</i>

*\* Solo acepta estudiantes de la Escuela de Medicina.*

examen autorizado por la AMA que ofrece la Escuela de Medicina de Puerto Rico. Se exigen calificaciones aceptables en evaluaciones mensuales y pasar un examen de ciencias clínicas para aprobar este curso.

Se puede solicitar la Quinta Trayectoria a:

Director de Educación Médica Continua  
Recinto de Ciencias Médicas  
G. P. O. Box 5067  
San Juan, P. R. 00936

Si el estudiante no aprueba el examen de ingreso para este curso, es aconsejable que se

dedique con ahinco a una revisión de Ciencias Básicas. El Curso de Actualización Médica, (vide infra), puede proveer un ambiente apropiado para esta revisión. Funcionar como voluntario en un hospital o trabajar como asistente de médico a tiempo parcial pueden ser orientadores hacia la meta de aprobar los exámenes de Ciencias Básicas sin restarle la energía y el tiempo requeridos para su estudio.

### Curso Teórico-Práctico

Este curso es parecido a la Quinta Trayectoria pero fue diseñado para el recién egresado de universidades que no requieren internado

y/o servicio social para expedir su título. Si el egresado no ha tomado el ECFMG ni la segunda y tercera partes de la reválida de Puerto Rico, puede tomar este curso clínico-aplicado que le ayudará a prepararse para aprobarlos. Este curso se ofrece al presente sólo en el Centro Médico de Mayagüez.

Para ser admitido se requiere haber aprobado la primera parte de la reválida o un examen sobre Ciencias Básicas preparado por la Escuela de Medicina de Puerto Rico. La Escuela de Medicina ofrece su examen periódicamente cuando un grupo de interesados lo solicita.

Este curso de capacitación es de tipo "modular", no tiene fecha fija de entrada o de salida y dura un período aproximado de seis meses. Si se aprueba la reválida o el ECFMG mientras se toma este curso, puede solicitarse inmediatamente un internado reconocido. Una experiencia de uno o dos meses en este curso es apropiada para médicos graduados que quieran actualizarse en un área específica de la medicina.

Para solicitar este curso se deberá escribir al:

Director de Educación Médica  
Centro Médico de Mayagüez  
Mayagüez, Puerto Rico 00708

Varios alcaldes de la Región Oeste ofrecen \$200.00 al mes a los participantes en este curso que se comprometan a hacer su período de servicio público con ellos después de terminar su internado. Al solicitar la aportación de los alcaldes la iniciativa propia cuenta mucho.

#### *Curso de Actualización Médica*

La Escuela de Medicina de Puerto Rico ofrece un Curso de Actualización Médica que está diseñado principalmente para el médico que quiere poner al día sus conocimientos profesionales. Este curso es apropiado para prepararse a tomar los exámenes de Reválida, el ECFMG o el examen de la Junta Nacional de Examinadores de Médicos ("National Boards"). El Curso empieza al presente en la primera semana de julio. El horario es de 8:00

a.m. - 12:00 m. y de 1:00 p.m. - 4:30 p.m., de lunes a viernes, con la tarde del miércoles libre. En él se estudian las Ciencias Básicas y Clínicas de cada sistema. El estudiante es evaluado continuamente para que en todo momento reconozca y pueda corregir sus deficiencias. El costo del curso es de \$1,000.00 pero se puede tomar y pagar por secciones.

Para solicitar este Curso se escribe a:  
Director de Educación Médica Con-  
tinuada  
Recinto de Ciencias Médicas  
G. P. O. Box 5067  
San Juan, Puerto Rico 00936

#### *El "Año" de Servicio Público*

Para poder obtener una LICENCIA PERMANENTE para ejercer la medicina libremente en Puerto Rico es indispensable trabajar un mínimo de un año y un máximo de dos años en el Servicio Público.

Este servicio puede ser en un hospital, un Centro de Salud, o agencia médica gubernamental, estatal o municipal. La asignación es hecha por el Secretario de Salud, después de consultar con el médico. Para el año de servicio público, como para el internado, el Tribunal extiende una licencia provisional indicando el lugar específico de su uso. El salario durante el año de servicio público es el de Médico I, (aproximadamente \$1,000.00). *Hacer un año de residencia en un hospital del gobierno de Puerto Rico ya no cuenta como un año de Servicio Público.*

#### *Estipendios*

Cambios de sueldo anuales son ahora la regla en vez de la excepción por lo tanto los estipendios mencionados son una guía imprecisa. El estipendio por internado en los hospitales de gobierno es de \$505.00 mensuales más subsidios de \$280.00 adicionales por hospedaje y comida cuando el hospital no los pro-



vee. En los hospitales privados se ofrece un estipendio al interno, que fluctúa entre \$505.00 y \$600.00 mensuales. Hay planes para ofrecer un estipendio a los estudiantes de la Quinta Trayectoria y al Curso Teórico Práctico de aproximadamente \$300.00 mensuales y de \$500.00 para aquellos egresados que trabajen como asistentes de médicos.

### Hospitales Disponibles para Internado

Hay 16 hospitales autorizados para ofrecer internado en Puerto Rico por el Tribunal Examinador de Médicos. Excepto por los hospitales de la Capital no ha habido dificultad en conseguir internados para personas debidamente cualificados. Un aumento en

plazas se ha proyectado para el año 1977-78 (véase Tabla).

### Referencias

1. Ley que regula la práctica de la Medicina en Puerto Rico, Ley Núm. 22 Bol. Asoc. Médica P. R. 66: 256, 1974.
2. Ramírez Rivera, J.: La Práctica de la Medicina en Puerto Rico: 1974, Buhití 5: 14, 1975.
3. Ley Núm. 14 junio 23, 1976 Bol. Asoc. Médica P. R. 68: 179, 1976.
4. Ramírez Rivera, J.: El Camino Real (Editorial). Bol. Asoc. Médica P. R. 65: 199, 1973.
5. Jiménez Méndez, Alejandro: ¿Por qué un Curso Teórico-Práctico para Graduados en el Extranjero? Bol. Asoc. Médica P. R. 65: 192, 1973.
6. C. H. William Ruhe, M. D.: "Policy on Eligibility of Foreign Medical Students and Graduates for Admission to American Medical Education", Memorandum to all Program Directors of Approved Graduate Training Programs, et al., dated March 22, 1975.

# DIGALO EN ESPAÑOL OR "SAY IT IN ENGLISH"

José Ramírez Rivera, MD, FACP y Braulio Quintero, MD

**Summary:** We have registered 97 medical expressions used frequently in the classrooms and medical wards of the Mayagüez Medical Center during one year and recorded their Spanish equivalent. We have noted the tendency of Puerto Rican physicians to use incorrectly Spanish and English, mixing both languages and replacing native words with anglicisms.

We translate literally from English to Spanish, pronounce incorrectly English terms and utilize expressions that are in reality linguistic hybrids. English is used for emphasis, as if an anglicism would be more eloquent as a means of transmitting an idea. We use English also because we ignore the technical Spanish term; its use could also indicate that the speaker is a snob.

We conclude that this linguistic tower of Babel is incomprehensible and not functional; it is absurd and ridiculous. We suggest a careful and conscious attitude in the use of English and Spanish.

**Resumen:** Hemos registrado noventa y siete (97) términos Médicos usados con alta frecuencia en las aulas y salas de Medicina del Centro Médico de Mayagüez durante un año y anotado sus equivalentes en castellano. Observamos la

tendencia del cuerpo médico de Puerto Rico a no utilizar con la debida corrección el español y el inglés, mezclar ambos idiomas y reemplazar palabras castizas por anglicismos.

Traducimos literalmente del inglés al español, pronunciamos mal las dicciones inglesas, utilizamos términos que son en realidad híbridos lingüísticos. El inglés se usa para dar más énfasis a la expresión, tal como si el anglicismo diera a la dicción más capacidad de transmitir la idea. Se usa el inglés también porque se ignora el término técnico hispánico; puede ser indicio de esnobismo de parte del hablante.

Concluimos que esta Babel lingüística es incomprensible e inoperante, y resulta absurda y ridícula. Sugerimos una actitud consciente y cuidadosa en el uso del inglés y el español.

En los círculos médicos de Puerto Rico se ha aceptado tácitamente, el uso de un lenguaje técnico, mezcla de español e inglés, que surge de la redacción forzosa de nuestros expedientes clínicos en inglés, de la interrelación entre las instituciones científicas de nuestra isla y las de Estados Unidos, y de una preparación profesional inadecuada para el empleo oral y escrito de nuestro vernáculo. Inhibe nuestro desarrollo lingüístico el que casi todas las publicaciones de medicina a que tenemos acceso están escritas en inglés. La constante traducción festinada de expedientes clínicos, notas de evolución y órdenes médicas del inglés al español, no ayudan

a nuestra formación ni en un idioma técnico ni en otro.

Aunque existen expresiones equivalentes en la lengua hispánica para muchos de los términos que usamos, preferimos el empleo del anglicismo, tal vez porque nos es más conocido, o porque el correspondiente término castellano nos parece menos efectivo. Intercalamos palabras y frases en inglés, a veces repitiéndolas en ambos idiomas para dar énfasis, para expresarnos con más claridad. Y hacemos el ridículo en foros internacionales, al no poder expresarnos sin múltiples apoyaturas anglosajonas.

No es este corto escrito un registro exhaustivo, sino una muestra de lo que se dice y de cómo debe decirse. Sugiere éste más cuidado y corrección en el uso de nuestros dos dignos y expresivos idiomas: *Escríbalo y dígallo en español*, o "Write it and say it in English".

### Método

Durante un período de doce meses: de mayo de 1975 a abril de 1976, recopilamos términos ingleses que escuchamos en las aulas y salas de medicina en el Centro Médico de Mayagüez. Seleccionamos aquellas frases o palabras repetidas, durante dicho año, por más de cinco personas. Excluimos los anglicismos de uso común en español.

Agrupamos estos términos de acuerdo con la especialidad y sub-especialidad médicas en las cuales su uso es más frecuente; en un encasillado aparte, agrupamos los términos de uso general que no pertenecen a las especialidades mencionadas. Anotamos siglas y frases en inglés junto a su término hispánico o traducción correspondiente y entre paréntesis, para *el entretenimiento y desorientación* del lector, hemos tratado de transcribir la pronunciación "inglesa" que a algunos de dichos vocablos se les da aquí.

Durante los doce meses en que llevamos a cabo esta pequeña investigación, integraban el cuerpo médico de medicina interna, de

veinticinco a treinta personas, incluyendo instructores médicos, residentes o internos y estudiantes de medicina de último año. Los miembros de este cuerpo médico provenían de los siguientes países y universidades:

### Puerto Rico — 14

Universidad de Puerto Rico  
Fac. de Medicina de Salamanca  
Fac. de Medicina de Santiago de Compostela  
Fac. de Medicina de Barcelona  
Universidad Central de Madrid

### Santo Domingo — 7

Universidad Nacional Pedro Henríquez Ureña  
Universidad Autónoma de Sto. Domingo

### Colombia — 3

Universidad de Cartagena  
Universidad de Antioquía  
Universidad Javeriana

### Méjico — 4

Universidad Autónoma de México  
Universidad Autónoma de Guadalajara  
Universidad de Monterrey

### Cuba — 1

Fac. de Medicina de Salamanca

### Argentina — 1

Universidad de Mendoza

### El Salvador — 1

Universidad de El Salvador

### Observaciones

*Cardiovascular*



A. S. D. = Auricular Septal defect — Comunicación Auricular

Acute M. I. = Infarto agudo (Aqiut emai)

B. P. = Blood Pressure — Presión arterial (bipi)

C. V. P. = Central Venous Pressure — Presión Venosa Central (civipi)

Chest Discomfort = Molestia en el pecho (ches disconfor)

Chest Pain = Dolor de pecho (ches pain)

E. K. G. = Electrocardiogram — Electrocardiograma (ekigi o ikeiyi)

Heart Rate = Frecuencia cardíaca (jart reit)

I. C. C. U. = Intensive Coronary Care Unit — Unidad de Cuidado Coronario Intensivo (aiciciyu)

I. C. U. = Intensive Care Unit — Unidad de Cuidado Intensivo

K. C. L. = Potassium Chloride — Cloruro de potasio (keiciel)

P. V. C. = Premature Ventricular Contractions — Prematuros; Contracciones Ventriculares Prematuras (pivici)

Sinus Arrest = Paro sinusal — (Sainus arres)

### *Endocrino*

Blood Sugar = Azúcar sanguíneo o Glicemia (blod shugar)

Cushing's Syndrome = Síndrome de Cushing (Cushin sindrom)

D. I. C. = Disseminated Intravascular Coagulation — Síndrome de Coagulación Intravascular diseminada (di ai ci)

Diabetes, Adult Onset = Diabetes, de comienzo adulto (daibetis adult ounset)

Diabetic Diet = Dieta diabética (diabetic daiet)

Fasting blood sugar = Glicemia en Ayunas

G. T. T. = Glucose Tolerance Test — Prueba de tolerancia a glucosa (yititi)

Inappropriate ADH Secretion = Secreción inapropiada de hormona antidiurética

Juvenile Diabetes = diabetes juvenil (Yuvenil diabetes)

Ketoacidosis = Cetoacidosis (quetoacidosis)

Two Hours Post Prandial = Dos horas postprandial (tu auars posprandial)

### *Gastrointestinal*

Barium enema = Enema de Bario (Barium Enema)

Chronic Active Hepatitis = Hepatitis Activa Crónica (cronic activ epataitis)

G. I. Bleeding = Gastrointestinal bleeding — Sangrado o hemorragia gastrointestinal (yiai bliding)

Jaundice = Ictericia (yaundis)

Levin Tube = Tubo de Levin (levin tiub)

Liver Scan = Escintigrama de Hígado o hepatogramagrama

Nasogastric Tube = Tubo Nasogástrico (nasogastric tiub)

P.. U. D. = Peptic Ulcer Disease — Enfermedad ulcerosa péptica (peptic olcer disis)

Rectal Exam = Tacto rectal (rectal ecsam)

Spleen Scan = Escintigrama de Bazo (splin scan)

### *Hematología*

A. G. L. = Acute Granulocytic Leukemia — Leucemia Granulocítica Aguda

A. L. L. = Acute Lymphocytic Leukemia — Leucemia Linfocítica Aguda

Blood indices = índices sanguíneos (blod indicis)

Bone Marrow = Médula Osea (bon marrow)

C. G. L. = Chronic Granulocytic Leukemia — Leucemia Granulocítica Crónica

CH. L. L. = Chronic Lymphocytic Leukemia — Leucemia Linfocítica Crónica

Dimorphic Anemia = Anemia Dimórfica (dimorphic anemia)

Hypoplastic Anemia = Anemia Hipoplástica

Iron Deficiency = deficiencia de hierro (airon difishensi)

Multiple Myeloma = Mieloma múltiple (multipol mieloma)

Peripheral Smear = Frotis o Extendido Periférico (periferal esmiar)

Platelet Count = Recuento de plaquetas (platelet count)

Shift to the left = desviación a la izquierda (shif tu di lef)

### *Laboratorio*

A. S. O. Titer = Antistreptolisin Titer — Título de Antiestreptolisina (aso taiter)

BUN = Blood Urea Nitrogen — Nitrógeno

Uréico Sanguíneo (bi iu en)

CBC = Complete Blood Count — Recuento Sanguíneo Completo (Hemograma Completo) (ci bi ci)

C. V. A. = Cerebrovascular Accident — Accident cerebrovascular (ACV) (ci vi ei)

Chronic Brain Syndrome = Síndrome Cerebral Crónico (cronic brein sindrom)

L. D. H. = Lactic Dehydrogenase — Deshidrogenasa Láctica (el di eich)

Pregnancy Test = Prueba de embarazo (pregnasi test)

S. G. O. T. = Transaminasa Glutámica Oxalacética (es yi ou ti)

S. G. P. T. = Transaminasa Glutámica Piruvica (es yi pi ti)

S. L.D. = Systemic Lupus Erythematosus — Lupus Eritematoso diseminado

Sedimentation rate = Velocidad de sedimentación (sedimenteishon reit)

Target Cells = Célula tipo del tiro blanco (target cel) Células en diana

### *Neurología*

C. V. A. = Cerebrovascular Accident — Accidente cerebrovascular (ci vi ei)

Chronic Brain Syndrome = Síndrome Cerebral Crónico (cronic brein sindrom)

E. E. G. = Electroencephalogram — Electroencefalograma (i i yi)

Minimal Brain Disfunction = Disfunción Cerebral Mínima

S. O. L. = Space Occupying Lesion — Lesión que ocupa espacio

Spinal Tap = Función Espinal — Función raquídea o Función lumbar (espinal tap)

Stroke = Derrame cerebral o Apoplejía (strok)

T. C. I. = Transient Cerebral Ischemia — Isquemia cerebral transitoria (ti ci ai)

### *Pulmonar*

Bird Respirator = Respirador tipo Bird (berd respireitor)

Blood Gases = Gases Arteriales (blod gases)

Bronchial Asthma = Asma bronquial (bronquial asma)

Bronchopneumonia = Bronconeumonía

Chest Film = Radiografía de Tórax (ches film)

Chest X-Ray = Radiografía de Tórax (ches exrei)

Coin Lesion = Lesion Numular (coin lision)

I. P. P. B. = Intermittent Positive Pressure Breathing — Respirador Intermitente a Presión Positiva (ai pi pi bi)

Lung Scan = Escintigrama de pulmón (lon escan)

Plate-like Atelectasis = Atelectasia en placas (plet laik atelectasis)

Pleural Effusion = Derrame pleural (pleural efiushion)

Rales = rales o estertores (reils)

Respiratory Distress = Dificultad respiratoria (respiratory distres)

Rhonchi = Roncus (roncai)

Wheezes = Sibilancias (juíces)

### *Radiología*

Barium Swallow = Esofagograma (Barium swallow)

Brain Scan = Escintigrama de cerebro (brein escan)

Chamber Analysis = Análisis de cámaras (Chainber análisis)

Gall Bladder Series = Colecistografía oral (gall bladder siris)

Skull Series = Estudio seriado del cráneo (escul siris)

Small Bowel Series = Estudio seriado del Intestino delgado (esmol bagüel siris)

Upper G. I. Series = Estudio de tracto gastrointestinal superior

### *Renal*

B. P. H. = Benign Prostatic Hypertrophy — Hipertrofia prostática benigna (bi pi eich)

G. F. R. = Glomerular Filtration Rate — Velocidad de Filtración Glomerular (yi ef ar)

I. V. P. = Intravenous pyelogram — Pielografía endovenosa (ai vi pi)

Hyperuricemia = Hiperuricemia (jaiperuricemia)

Low Salt Diet = Dieta baja en sal (lou sol daiet)

Nephrotic Syndrome = Síndrome Nefrótico (nephrotic sindrom)

Salt Losing Nephritis = Nefritis Perdedora de



sal (solt lusin nepritis)

U. T. I. = Urinary Tract Infection — Infección de tracto urinario (yi ti ai)

### Uso General

Absolute Bed Rest = Reposo absoluto en cama

Approach to the patient = acercamiento al paciente

Available = Disponible (availabol)

Background = transfondo o antecedentes

Blind Spot = Punto Ciego (blain spot)

Blood Cultures = Cultivos de sangre (Blod colchurs)

Bound to Protein = Unido a proteínas

CPC = Clínico Pathologic Conference — Conferencias Clínico-Patológicas (ci pi ci)

Cause Undetermined = Causa Indeterminada (cos ondetermin)

Cause Unknown = Causa Desconocida (cos onnoun)

Cluster = Acúmulo

Cuff de Presión = Manguito de Presión

Chief Cells = Células Principales

Chief Complaint = Queja principal (chif com-plein)

E. R. = Emergency Room — Sala de Emergencias (emergenci rum)

Fatty Casts = Cilindros grasos

Feed Back = Retroalimentación (fidbac)

IV Fluids = Intravenous Fluids — Líquidos Intravenosos o endovenosos (ai vi fluids)

Handicap = impedimento (jandicap)

In the Chart = En el récord (in char)

Incident Report = Informes de incidentes (incident riport)

Journal Club = Club de Revistas — Revisión de Trabajos (Yournal clob)

Malignancy = Malignidad (malignanci)

Morning Report = Informe matutino (mornin riport)

Nurses Notes = Notas de Enfermería (Norses nouts)

Nursery = Sala de recién nacidos

Oval Fat Bodies = Cuerpos Grasos Ovais

P. O. R. = Problem Oriented Record — Expediente Orientado al problema (pi o ar)

Problem List = Lista de problemas (problem list)

Progress Notes = Notas de evolución (progres nout)

Protein Binding Capacity = Capacidad de Unión a proteínas

Rule Out = Descartar (rul aut)

Squamous Cell CA = Carcinoma de células escamosas

Threshold = dintel

Tube Feeding = Alimentación por tubos (tiub fiding)

Upset = molesto (opset)

Unreliable = No confiable (onrilaibol o onri-  
liabel)

Until Proved Otherwise = Hasta que se pruebe  
lo contrario (ontil pruvd oder wais)

### Comentarios

Dentro del marco de las necesidades de salud de Puerto Rico expresarse mejor no debiese tener una prioridad alta. Pero si la expresión clara y precisa es consecuencia natural de un pensar lógico y ordenado, creemos que el momento está llegando en que nos dirijamos en esa dirección.

Observamos y señalamos la tendencia del cuerpo médico de Puerto Rico a utilizar incorrectamente tanto el español como el inglés, a mezclar ambos idiomas y a reemplazar voces técnicas españolas por inglesas. Estas dos últimas tendencias, errónea e inconscientemente obedecen a una intención de dar más énfasis a la expresión, tal como si el anglicismo diera a la dicción una mayor capacidad de transmitir la idea. Podrían también obedecer a una actitud de esnobismo del hablante o a una ignorancia injustificada del término hispánico.

Traducimos literalmente al español, por ejemplo: "history of" lo traducimos como 'historia de' en lugar de 'historial de'; reemplazamos continuamente la voz española: ej. "Barium enema" por 'enema de bario', pronunciamos mal las dicciones inglesas como 'escul siris' por "skull series", y por último, utilizamos términos que

son en realidad híbridos lingüísticos, como GI Bleeding y R/O várices esofágicas.

El resultado es una *Babel* lingüística, absurda y ridícula, comprensible únicamente para un núcleo mínimo y limitadísimo aún dentro de Puerto Rico e inoperante e incomprensible en cualquier medio hispánico o anglosajón, fuera de Puerto Rico.

No es nuestro propósito modificar en su totalidad el arraigado sublenguaje que usamos. Aceptamos que frases que al inicio se codifican como signos de barbarie terminan siendo aceptadas por su insustituible brevedad y lucidez. Pero creemos también que nuestra incorporación del inglés al vernáculo excede nuestra capacidad para amoldar y disciplinar el vocablo foráneo para una mejor transmisión de ideas; más, dentro de nuestro contexto hispanoamericano vemos esta tendencia como oscurantista.

No pretendemos con este estudio cambiar de una pincelada los hábitos lingüísticos del cuerpo médico. Nuestro propósito es más humilde: Queremos alentar el refinamiento de nuestras destrezas idiomáticas para una mejor comunicación. Deseamos destacar una realidad que suele pasar por inadvertida, pero que el reconocerla puede y debe llevarnos a corregir los errores que cometemos. Aspiramos a desarrollar una actitud consciente y cuidadosa en el uso de ambos idiomas, lo que redundará en prestigio y respeto para nuestra clase médica.

### Agradecimiento

Agradecemos al Dr. Ramón Luis Deza y el Dr. Frank Gaudier, por sus sugerencias y su ayuda en la corrección del manuscrito.

## POLIPOS DE LA URETRA POSTERIOR

Juan R. Iturregui-Pagán, M.D. y Roberto F. Fortuño, M.D.

**Abstract:** A case of posterior urethral polyp in a sixteen month old boy is presented. The pathological classification and clinical characteristics of the 44 cases that have appeared in the world literature are summarized and discussed.

**Resumen:** Se presenta el caso de un niño de 16 meses de edad con un pólipo de la uretra posterior. Se discute la clasificación y características clínicas de los 44 casos descritos en la literatura mundial.

Los pólipos de la uretra posterior son lesiones extremadamente raras del sistema genito-urinario masculino, pero se conoce su existencia desde hace más de un siglo (1). Sir Henry Thompson en 1885 publicó el primer caso descubierto en una autopsia (2). En 1872 Tarnowsky reportó el primer caso diagnosticado en un sujeto vivo (3) y Neuberger en 1899 hizo el primer diagnóstico endoscópico (4).

Diferentes investigadores han clasificado estas lesiones de acuerdo con su composición histopatológica. Randall (5) los dividió en fibrosos, vilosos y glandulares. A estos Nesbit (5)

le añadió un cuarto tipo que incluía pólipos con tejido prostático aberrante. Preferimos la clasificación de Mostofi (7) que los divide en tres grupos: a saber:

- (1) Uretritis polipode que son pólipos muy similares a y con los mismos factores etiológicos de la cistitis polipoide. Se componen de células inflamatorias y vasos sanguíneos dilatados con algunos o todos los cambios de la cistitis proliferativa.
- (2) Pólipos fibrosos de configuración estrecha que se originan de la uretra cerca del verumontanum. El cuadro histológico es similar al de la uretritis polipoide pero sin el componente inflamatorio.
- (3) Los pólipos adenomatosos se componen de tejido columnar alto parecido al de las glándulas prostáticas. Algunos creen que estos pólipos se originan de evaginaciones pedunculares de acinis glandulares, (6, 7, 8) este tipo se ha descrito solamente en adultos (5, 7, 8).

### Presentación de Casos

---

*Del Departamento de Urología del Hospital Municipal de San Juan y la Sección de Urología de la Escuela de Medicina, Universidad de Puerto Rico.*

El 4 de marzo de 1975 se admitió al servicio de urología pediátrica del Hospital Municipal de San Juan





Figura 1: Cistometrograma demostrando el pólipo en la uretra posterior.



Figura 2: Vista endoscópica del pólipo uretral mostrando su relación con la porción anterior del cuello vesical.



Figura 3: Pólipo de uretra posterior, vista macroscópica.



Figura 4: Pólipo de uretra posterior, vista microscópica.

un niño de 16 meses con historial de una semana de hematuria macroscópica silenciosa y terminal. El niño no tenía historial de problemas urinarios previos, ni ningún otro problema nrológico o sistémico. El historial pasado, repaso por sistema y examen físico no revelaron hallazgo positivo alguno. El pielograma intravenoso era normal. El cistouretrograma demostró un defecto en llenado de forma alargada en la uretra posterior que variaba su posición con el fluir de la orina. La uretra posterior no estaba dilatada y la vejiga parecía normal sin evidencia de reflujo vesico-ureteral (Fig. 1). La cistouretroscopía reveló una vejiga y uretra

**TABLA I**  
**DISTRIBUCION POR EDAD**

	<i>Número</i>	<i>Por Ciento</i>
<i>0-12 años</i>	2	5
<i>1-6 años</i>	23	52
<i>7-14 años</i>	8	18
<i>15-21 años</i>	4	9
<i>22-40 años</i>	3	7
<i>41-60 años</i>	3	2
<i>No indicado</i>	1	2
<i>Total</i>	44	100

**TABLA II**  
**SIGNOS Y SINTOMAS**

	<i>Número</i>	<i>Por Ciento</i>
<i>Dificultad al Orinar</i>	31	70
<i>Hematuria</i>	13	29
<i>Enuresis</i>	5	11
<i>Infección tracto urinario</i>	2	5
<i>Uremia</i>	1	2
<i>Descarga uretral</i>	1	2

anterior normal; en la uretra posterior notamos un pólipo alargado de superficie lisa con algunas ulceraciones que se originaba del verumontanum y proyectaba hacia la vejiga urinaria (Fig. 2). Resecamos esta lesión por vía endoscópica y se fulguró su base. El examen histopatológico reveló una lesión polipoide de 1.2 por 0.3 cm cubierta por tejido transicional y compuesto de un área central fibromuscular con vasos dilatados (Figs. 3, 4).

Desde esta intervención el niño ha continuado completamente asintomático. Urocultivos y urinalisis repetidos han sido negativos. Se ofreció una cistoscopia

para control post-operatorio, pero el procedimiento no fue aceptado por los padres del niño.

### Discusión

Incluyendo este caso, se han presentado en la literatura mundial 44 casos de pólipos fibrosos de la uretra posterior (1, 9-22). Las características clínicas de todos estos enfermos se

TABLA III  
HALLAZGOS RADIOGRAFICOS

	Número	Por Ciento
<i>Tracto Superior normal</i>	22	50
<i>Dilatación tracto superior</i>	10	23
<i>Estado de tracto superior no indicado</i>	12	27
<i>Divertículos vesicales</i>	4	9
<i>Reflujo vesico-ureteral</i>	3	7

TABLA IV  
TRATAMIENTO

	Número	Por Ciento
<i>Excisión supravesical</i>	21	48
<i>Resección transuretral</i>	21	48
<i>No tratados (hallazgos de autopsia)</i>	2	4

resumen en las siguientes tablas:

La Tabla I demuestra que las edades varían de 21 días a 59 años, pero que más de la mitad de los casos ocurrieron en niños pre-escolares.

Setenta por ciento de los casos se presentaron con signos y síntomas de obstrucción vesical y la mayoría de éstos tenían infección urinaria. En solo en un 29 por ciento la queja principal fue hematuria.

Como en otros tipos de obstrucción vesical, el aspecto más importante en el pronóstico de estas lesiones es la condición de los tractos urinarios superiores. En 23 por ciento de los casos había daño renal en el momento del diagnóstico; en 27 por ciento de los casos la condición del tracto urinario superior no fue informada y en el resto tenían tracto superiores normales.

Otros hallazgos radiográficos incluyen divertículos vesicales en un 9 por ciento y reflujo vesico-ureteral en un 7 por ciento.

La Tabla IV resume las varias formas de tratamiento para estas lesiones. Se usó la excisión transvesical suprapúbica en 48 por ciento y un número igual fue resecado por vía transuretral. Es importante notar que desde el 1968 la forma más común de tratamiento (75 por ciento) ha sido la resección endoscópica. El 2 por ciento de estos pacientes no recibieron tratamiento ya que fueron diagnosticados por examen post mortem.

Nuestro caso no es típico ya que el niño no presentaba signos de obstrucción urinaria y su único síntoma fue hematuria. El paciente respondió bien a la resección transuretral de la



lesión, la cual creemos será el método preferido de tratamiento.

### Referencias

1. Barrie, H. J. and Simons, D. C.: Hydronephrosis Resulting from Obstruction of the Urethra by a Polyp of the Verumontanum. *Am. J. Clin. Path.* 36: 356 (1961).
2. Thompson, H.: Stricture of the urethra. *Transactions of the Path. Soc. of London*, 7: 250 (1855).
3. Tarnovsky: Vortage uber venenische Kramkheinten, Berl. (1872).
4. Neuberger, J.: Butrag. zue Lechre vou den Polypen der Harnrohre. *Wiener Medizinische Presse*. 30: 897 (1889).
5. Randall, Alexander: A. Study of the Benign Polyps of the Male Urethra. *S. G. O.* 17: 584 (1913).
6. Nesbit, Reed: The Genesis of the Benign Polyps in the Posterior Urethra. *J. Urol.* 87: 416 (1962).
7. Mostofi, F. K. and Price, E.B.: Tumors of the Male Genital System, Washington, A. F. I. P., 1973, pp 263-266.
8. Butternik, James, Schitzer, Bertrand, and Abell, Murray: Ectopic Prostatic Tissue in the Urethra. A Clinicopathological Entity and a Significant Cause of Hematuria. *J. Urol.* 105: 97 (1971).
9. Downs, Ralph A.: Congenital Polyps of the Prostatic Urethra. *Brit. Jour. Urol.* 42: 76 (1970).
10. Dewolf, W. C., and Fraley, Etwin E.: Congenital Urethral Polyp in the Infant: Case Report and Review of the Literature. *J. Urol.* 109: 515 (1973).
11. Roller, Mark and Naranjo, Carlos: Benign Urethral Polyp of the Prostatic Urethra. *Urology* VI: 34 (1975).
12. Braun, Edward: Congenital Polyp of the Prostatic Urethra in a Child. *J. Urol.* 114: 311 (1975).
13. Campbell, M. F.: *Urology*, Philadelphia, W. B. Saunders Co., 3 ed., 1970 p. (1926).
14. Carter, Michael: Polyp Granuloma Pyogenicum of the Posterior Urethra. *J. Urol.* III: 616 (1974).
15. Flanagan, Malachi, Keefer, Joseph, and McDonald, James: Pendunculated Solid Polyps of the Posterior Urethra. *J. Urol.* 90: 200 (1963).
16. Gatewood, Olga M., Calhoun, Robert L., and Levin, Sidney: Pendunculated Polyps of the Posterior Urethra. *J. Urol.* 97: 1052 (1967).
17. Medows, James A. and Quattlaum, R. B.: Polyps of the Posterior Urethra in Children. *J. Urol.* 100: 317 (1968).
18. Mogg, Richard: Congenital Anomalies of the Urethra. *Brit. J. Urol.* 40: 638 (1968).
19. Scott, W. F., Collins, T. A. and Singer, P. L.: Papilloma of the Urethra in an Infant. *Jour. Med. Asso. Ala.* 7: 370 (1938).
20. Stueber, Paul, and Persky, Lester: Solid Tumors of the Urethra and Bladder Neck. *J. Urol.* 102: 205 (1969).
21. Williams, D. I. and Abbassian, A.: Solitary Penduculated of the Posterior Urethra. *J. Urol.* 96: 483 (1966).
22. Nallans, Roger E. and Stein, Jay: Pedunculated Polyp of Posterior Urethra. *Urology* VI: 474 (1975).

## **LA ESCUELA DE MEDICINA ANTE LA EDUCACION MEDICA CONTINUADA**

*Por sexta vez consecutiva en la Escuela de Medicina comenzó en el verano de 1976 un curso formal de educación médica continuada de seis meses de duración.*

*Los orígenes de la actual actividad de Educación Médica Continuada de la Escuela de Medicina de Puerto Rico datan del año 1968 cuando el entonces Decano Sifontes preparó una propuesta basada en las recomendaciones del Comité de Educación Médica Continuada presidido por el Dr. Antonio Ortiz. Esta fue favorecida por un donativo mediante un contrato entre el Centro Nacional de Investigación en Servicios de Salud del Departamento de Salud federal y la Escuela de Medicina. Este contrato fue adjudicado por tres años e hizo posible que la Escuela ofreciera los primeros tres Cursos de Perfeccionamiento entre los años 1970 y el 1973.*

*La misión principal de estos cursos era ofrecer la oportunidad a médicos en Puerto Rico, que habían fracasado en sus pruebas de Reválida o en el "ECFMG", de prepararse para dichos exámenes.*

*A través de los primeros tres años de existencia de este Curso, se pudo lograr que cerca de 100 médicos muchos de ellos empleados de instituciones del gobierno, pudiesen capacitarse para ejercer legalmente la medicina en Puerto Rico. Así pudieron extender sus servicios a un mayor número de miembros de la comunidad puertorriqueña.*

*Fue este un logro en la educación médica del país tan significativo que el Departamento de Salud de Puerto Rico se interesó en continuar auspiciando el Curso una vez terminado el contrato original.*

*A partir de febrero de 1975 la Escuela de Medicina asumió la responsabilidad económica de la actividad. Consciente de las nuevas necesidades en Puerto Rico por programas en educación médica continuada, la Escuela aprovechó esta oportunidad para crear una División de Educación Médica Continuada bajo la Oficina del Decano de Medicina. El Curso se convirtió en una de las actividades principales de esta recién creada división. Se le dió una nueva orientación y un nuevo nombre — Curso de Actualización Médica.*

*Dicho curso consta ahora de dos partes: Ciencias Básicas y Ciencias Clínicas. El Curso se ha preparado en módulos con objetivos de aprendizaje bien definidos, de tal forma que médicos interesados pueden aprovechar el Curso entero durante sus seis meses de duración, o porciones del mismo, según sean sus intereses o necesidades particulares. Así, médicos en la práctica pueden actualizar sus conocimientos en temas especiales como gastroenterología, o en enfermedades infecciosas; según otros pueden utilizar el Curso para prepararse para los exámenes de la reválida de Puerto Rico, el "ECFMG" o el "FLEX".*

*Las recientes modificaciones de la ley de la práctica de la medicina en Puerto Rico imponen a las actividades de educación médica continuada y al Curso de Actualización Médica nuevas responsabilidades educativas. La enmienda que establece como requisito haber aprobado la Primera Parte de la Reválida antes de comenzar el médico su primer año de adiestramiento postgraduado (internado—*

requisito de ley) es un ejemplo. El Curso de Actualización Médica ofrece la oportunidad a estudiantes de medicina que hayan terminado sus requisitos de Ciencias Básicas en escuelas de medicina de prepararse para estos exámenes.

Otro ejemplo que acrecentará extraordinariamente la importancia de la División de Educación Médica Continuada es la nueva ley de Reforma Integral de los Servicios de Salud de Puerto Rico de 1976. Esta ley establece los requisitos y los mecanismos para el registro cada dos años y la recertificación periódica de profesionales en base a educación médica continuada según lo determine el Tribunal Examinador de Médicos de Puerto Rico en su reglamento. Sin lugar a dudas, la implantación de esta ley hará cada día más necesarias las actividades de educación médica continuada bien planeadas, de gran excelencia y correctamente evaluadas.

En este número del Boletín, los doctores Colón-Rivera, Sifontes y el Sr. Donald W. Keillor presentan una fase crucial en el desarrollo de los primeros Cursos de Perfeccionamiento que se ofrecieron. Señalan ellos los conceptos utilizados para la evaluación del contenido de los Cursos, sus objetivos, la preparación de los mismos y, sobre todo, las ejecutorias de los médicos que se beneficiaron de ellos. Establecen claramente los autores el continuo círculo en los procesos educativos de: definición de objetivos de aprendizaje → desarrollo de los programas y experiencias de aprendizaje → evaluación de todo el proceso . . . . . , y de vuelta a los objetivos.

Fueron estos conceptos, empleados tan eficaz y eficientemente en el Curso de Perfeccionamiento, los que sirvieron de base para la creación del currículo actual de la Escuela de Medicina sobre bases educativas científicas y sólidas.

Es evidente que la educación médica en Puerto Rico le debe mucho a las primeras experiencias con el Curso de Perfeccionamiento y con sus procesos evaluativos.

Carlos E. Girod, M. D.



## TEXT BOOK OF BLACK RELATED DISEASES

by Richard Allen Williams  
MacGraw Hill editors (1975)

This book is an important addition to the medical literature. Indeed, it appears to be the first book to show the characteristics of diseases for each organ as they occur in black people. It relates to diseases only seen in the black community (i.e., sickle anemia) as well as the changing aspects that other ethnic diseases can take in this community. In fact we have to consider this book as a book of "comparative medicine".

Dr. Richard ALLEN WILLIAMS editor in chief of this remarkable book explains clearly in the preface the aim of this work. The idea of the book came to him at Harvard Medical School when students make him notice that "they would not be adequately prepared to treat the underprivileged minorities because they would not have received proper training about the diseases to which the latter groups are prone". From this consideration he was driven to realize that "standard medical text-books contain almost nothing relating to the special medical problems of underprivileged minorities" so that the health care needs of minority groups were being interpreted and analyzed from the perspective of the majority groups". All these reflexions must lead him to write this book of which the long range goal is to introduce a new discipline we can call "ethnic medicine".

Written by twenty five authors the book has twenty chapters treating all the conventional divisions of medicine except Rheumatology

and Nephrology.

It is obvious that the book was written for the American black community and we can not be surprised not to find diseases affecting African Negroes but unknown in U. S. A. (Schistosomiasis, trypanosomiasis...).

There is no mention of a possible ethnic repartition of H. L. A. groups.

There is a very exciting paper on "voodoo medicine".

Sickle cell anemia is treated in almost every chapter which is quite normal according to such a polymorphus disease.

The chapter about cardiology was written by R. ALLEN WILLIAMS himself and is surprising the lack of development of Rheumatic disease fever, known to be a dramatic problem in underprivileged groups of U. S. A.

Hypertension is widely studied. It seems to be more precocious, more frequent and more severe problem in American black people than in white people. Strokes seem more frequent than coronary complications. Similar data have been reported in African publications.

Docteur Alain LOUIS-GUSTAVE  
Martinique  
French West Indies

*FROM THE DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE*

*AGING: A CHALLENGE TO MEDICINE*

The health care system and other vital American institutions were not prepared for the demographic revolution of the 20th Century that saw the population of older Americans grow seven-fold while the general population only tripled.

This human triumph of increased life expectancy is clouded by the situation created because the nation was not prepared for a "sudden" increase of citizens 65 and older — from 3 million in 1900 to 23 million today.

The major task before the nation is to adapt its social institutions to the needs of older people while, at the same time, it meets the needs of the younger population.

The prospect of the older population growing to 30 million by the year 2000 poses an especially serious challenge to the health care profession — from the "pure" research scientist in the laboratory to the practitioner in his consulting room.

The profession is ill-prepared to meet that challenge, as indicated by a lack of training in geriatric medicine — not even fundamental education in this field is offered by American schools of medicine.

A survey of 99 medical schools in 1970, for example, found that 50 made no mention of geriatrics in their offerings. And, of the nation's 114 medical schools, only 32 offer electives in the subject.

Until January of this year the nation in which one out of every 10 citizens is 65 years of age and older had not a single endowed chair in geriatric medicine. Today, there is one — the Irving Sherwood Wright Professorship in Geriatrics at the New York Hospital-Cornell Medical Center in New York City.

Let us hope that establishment of that chair, by a \$1 million endowment from the Gladys and Roland Harriman Foundation, signals a new academic

emphasis and that the Wright Professorship is the first in a series of similar teaching and research positions to provide needed leadership in geriatrics throughout the country.

Medical education today is marked by serious shortcomings: No medical school requires that all its students receive part of their training within nursing homes, long-term care institutions, or in home-care programs. There are but two formal medical school training programs in geriatric medicine and very few centers in which any sort of training for research in clinical gerontology can be obtained. In other words, medical students get little or no sophisticated teaching regarding the medical problems of the elderly. This lack is reinforced by a prejudice toward the aged often displayed by teaching and practicing physicians.

The obvious conclusion is that the medical profession, as represented by its educational establishment, is not preparing itself to serve a rapidly growing population with special needs for health care that become more pressing every year.

There are indications that the general public is moving ahead of the medical profession in recognition of the special problems of the elderly and in taking action to solve them. Congress, as representative of the people, established the National Institute on Aging (NIA) as the 11th of the National Institutes of Health after finding that: "No American institution . . . has undertaken comprehensive systematic and intensive studies of the biomedical and behavioral aspects of aging and the related training of necessary personnel."\*

The Institute, which began operations last year, sees its main role as correcting this lack by supporting a comprehensive program of research and training on the variety of factors — biological, medical, social and behavioral — which contribute to the aging process. This research program is intended to produce the knowledge needed to prevent, modify or reverse the harmful aspects of aging and enhance the quality of the later years.

Institute scientists are working to distinguish aging from disease; identify the normal biological changes that accompany aging; understand the relationships between the aging process and the diseases related to advanced age; determine the psychological and social phenomena that contribute to and accompany changes with age; and develop the diagnostic, treatment and preventive procedures to apply this knowledge.

Research lies at the heart of solving such questions because, whether it is called basic or applied, research is the ultimate service. A comprehensive research plan was prepared by the Institute for the Department of Health, Education, and Welfare and presented to Congress, at its direction, earlier this year. The plan, entitled *Our Future Selves: A Research Plan Toward Understanding Aging* is designed to focus the resources of the government on all aspects of aging.

We recognize that research alone cannot accomplish the objective of a healthier and stronger older population, but the plan was offered as a reasonable and reasoned promise of a major endeavour to comprehend the nature of aging and its associated ills, with the ultimate aspiration of a more decent and dignified old age.

Far too many people, including professionals, see old age primarily as a time of chronic illness, failing mental abilities, dwindling bank accounts and stagnation. The vision of the plan extends beyond these concerns to the positive aspects of aging. Therefore, two basic ideas underlie the recommendations of the plan:

- \* Effective programs for the aged — whether medical or social, treatment or prevention — must be based on knowing which changes in the aged are intrinsic to the aging process and which are not.
- \* If we are able to prevent or lessen the impact of non-intrinsic factors in the decline of the aged, then we are left with a unique and more satisfying concept of what aging is or should be — a natural stage in human development leading to a gradual and peaceful end.

Through research, and with the support of medical schools and physicians, knowledge can be increased and applied to serve the elderly.

The readiness of the medical community to join in this effort was indicated by a survey of practicing

physicians, reported in the AMA's *IMPACT* (September, 1976), in which 75 percent of respondents answered affirmatively to the question: "Do M.D.'s need special training in geriatrics?" Such training would, for example, make more physicians aware that in the later years multiple disorders are present as the body's protective mechanisms are compromised. Symptoms present differently in the old and the untrained clinician often misses the diagnoses:

- \* An older person with hyperthyroidism may appear apathetic, not hyperactive.
- \* Tuberculosis may proceed in silence.
- \* Appendicitis may occur without the characteristic abdominal tenderness at Mc Burney's point, without fever, and without an elevated white count.
- \* An older person may have a heart attack without chest pain and may instead appear confused, disoriented and seem like the victim of a stroke.

In the area of drugs, most practitioners have at some time been distressed by the adverse and often paradoxical reactions and interactions that occur because of multiple drug use by older people. Even so, the classic Goodman and Gilman textbook does not even have the word "age" in its index. Beleaguered by many other demands, the Food and Drug Administration has never really concentrated on the special variables of age, despite our knowledge that with age and with the severity of disease, the impact and the acute and long-term toxicity of drugs is altered. We know far too little about the age — and disease — related effects of the 1,500 different drugs prescribed each year. For example:

- \* The dosage of the anticoagulant warfarin needs to be lessened when given to a person taking chloral hydrate.
- \* There is a greater risk of bleeding when heparin is administered to women.
- \* There appears to be a link between reserpine and breast cancer in women.
- \* Diazepam causes excessive drowsiness with



age.

Learning more about various medications and their age-related effects is one type of basic research appropriate for the NIA. We need wise prescription guidelines in our work with older people, but first we need the scientific knowledge to enable us to develop such guidelines.

The special effect of diet on the condition of the elderly is not well enough understood. Nutrition has been shown to be the only environmental factor to increase the life span in animal model systems. Unfortunately, the nutritional status of aged persons is often poor. Undernutrition can be the key to an array of pathologies, such as intellectual confusion (so-called senility), and anemia, which could be reversed if adequate nutrition were provided. However, what constitutes "adequate nutrition" for aged persons is not fully known.

Most information on nutritional needs is based on research with children and young adults. But, because of changes in the physiology of the aged, such information is not likely to be applicable to the needs of this group. It would be of tremendous benefit to the aged to have valid guidelines for their nutritional requirements, including the need for vitamins, trace elements, fats, carbohydrates and proteins.

The Institute actively seeks the support of the medical community and public and private agencies to increase the total resources available to accomplish its research goals and to bring the old into the mainstream of American medicine.

---

#### NEW TREATMENT PREVENTS SERIOUS DISEASE OF PREMATURE INFANTS

CHICAGO — A new treatment to prevent hyaline membrane disease — a serious respiratory disorder in premature newborns — is described in the April 25 Journal of the American Medical Association.

A research project at Roswell Park Memorial Institute, Buffalo, N. Y., confirmed that administration of plasminogen — a substance extracted from human blood — within 60 minutes of birth brings a substantial decrease in severe breathing problems and in death from hyaline membrane disease in premature newborns.

The most common cause of death in both premature and full-term infants in the hours following birth is respiratory difficulty. About half such affected infants are found to have an excess of pink fluid clinging to the membranes of the bronchial tubes. This condition is called hyaline membrane disease (HMD).

Statistical studies have shown that HMD and respiratory distress is the underlying cause of death in some 9,000 infants each year, approximately 20 percent of all neonatal deaths.

Clara M. Ambrus, M. D., of Roswell Park Memorial Institute, and colleagues report on a study involving 500 premature infants. Half were treated within an hour of birth with plasminogen. Half received a placebo. The patients were in four hospitals affiliated with the State University of New York at Buffalo. In each hospital the study was approved by the Committee on Human Experimentation.

In the 249 infants in the placebo group, 22 had mild and 31 severe respiratory distress. Of the last 31, twenty died; 11 had HMD. In the plasminogen-treated group of 251 infants, mild respiratory distress developed in 35 patients and severe respiratory distress developed in 19. This is the reverse of the ratio observed in the placebo group, Dr. Ambrus points out. Of the latter 19, six died.

Administration of plasminogen did not change the overall occurrence of respiratory distress in premature infants, but its use often converted a potentially serious disease into a mild one of short duration requiring minimal care, the report says.

Plasminogen is given in a single intravenous injection shortly after birth. It can be administered by the family physician, obstetrician, or pediatrician, and a sophisticated intensive care unit is not required.

Mortality caused by HMD in the plasminogen group was about one-fourth that in the placebo group, Dr. Ambrus says.

---

#### SEXUAL REVOLUTION REFLECTED IN MEDICAL PRACTICE IN U. S.

CHICAGO — The so-called sexual revolution of the past 10 to 15 years is real, America's doctors report.

Two-thirds of primary care physicians responding to an American Medical Association poll declare that the sexual revolution has been "markedly reflected"

in their day-to-day office practice.

The doctors report an increase in requests for birth control information, more requests for abortion information, more incidence of venereal disease, and more requests from patients for help with sexual problems.

Results of the poll are published in the April 25 Impact Section of American Medical News, the AMA's weekly newspaper for physicians.

Doctors polled included general and family practitioners, internists, obstetricians-gynecologists, and pediatricians.

Some of the doctors report they are seeing more sexually related infections and diseases. Many more female patients are now taking the birth control pill. More requests are being received for sterilization, and doctors are being asked about sex after heart attacks. Teenagers are less reluctant to be examined than in the past, and there are more births to younger parents. More teenagers ask for sexual counseling.

---

#### HEMORRHOIDS TREATED SUCCESSFULLY BY SIMPLE, INEXPENSIVE TECHNIQUE

CHICAGO — Hemorrhoids can be safely and effectively removed by ligation with rubber bands at a cost of \$175 instead of by conventional surgery at an average cost of \$1,400, says a report in the April issue of the Archives of Surgery, a scientific publication of the American Medical Association.

Not only is the cost less, but the hospital stay of several days and the acute post-operative pain and discomfort is virtually eliminated, say John Bartizal, M. D., and P. A. Slosberg, M. D., of Loyola University, Chicago.

Ligating hemorrhoidal tissue by rubber bands has been used for 20 years as an alternative to regular surgery, they point out. The rubber band at the base of the hemorrhoid cuts off the blood supply, and the tissue sloughs off in a few days.

The Chicago doctors gave the technique a thorough test. Their report is a review of 670 patients who underwent 3,208 rubber band ligations for internal hemorrhoids. Mild to moderate discomfort occurred in 32 patients, while pain severe enough to limit activity occurred in only four patients. Slight bleeding was noted in 19 patients and severe bleeding in nine. Only

two of these nine required hospitalization and further treatment.

The bands were placed by an instrument used in the doctor's office. Most patients required six bandings for multiple hemorrhoids. And 98 percent of the patients got rid of their hemorrhoids with no complications sufficient enough to interfere with daily activity.

"Rubber band ligation of hemorrhoids meets all the requirements of an acceptable alternative to hemorrhoidectomy, and considering convenience, comfort, and cost, it may well be a superior alternative," say Drs. Bartizal and Slosberg.

The \$1,400 average cost of conventional surgery includes the physician's fee, hospital charges, and laboratory and X-ray charge. The \$175 cost for banding includes six bandings and proctoscopic examination.

---

#### AMA PROPOSES INCREASES IN CARTER HEALTH BUDGET

CHICAGO — The American Medical Association has suggested a series of increases in President Carter's budget proposals for various health programs.

In letters to Congressional leaders, the AMA said it was limiting its recommendations for additional appropriations that would increase the President's budget to "those programs that have the greatest promise for prevention and cost effectiveness to patients, because we realize that economic conditions have put an exceptional strain on scarce federal resources."

The AMA said that much more than the amount it has recommended was needed in some areas, but emphasized its conviction that "no less than the amounts recommended for these programs" should be appropriated.

Since many of the programs emphasize preventive care and are very cost effective, "they represent the best use of scarce fiscal resources," the AMA said.

Among the AMA recommendations:

*Maternal and Child Health* — The AMA recommends a \$50 million increase over the President's budget figure of \$345,424,000, providing a total of \$395,424,000. This additional amount would allow the states to extend and improve health services for mothers and children, as well as providing additional services to crip-

pled children.

*Family Planning* — The AMA requests an increase of \$17 million over the President's budget of \$123,165,000. This would provide a total of \$140,165,000, enabling this successful program to expand provision of family planning services to financially disadvantaged and high risk individuals.

*National Health Services Corps* — The AMA has long supported the NHSC as an effective means of delivering health care to shortage areas. To expand the scope of NHSC activities, we suggest that the President's request of \$37,590,000 be increased by \$8 million. This provides a total amount of \$45,590,000.

*Emergency Medical Service* — We recommend that the President's request of \$33,625,000 be increased by \$15 million to \$48,625,000. This additional amount would continue the effort to establish and improve emergency medical services throughout the nation.

*Immunization and Venereal Disease Programs* — The AMA requests an additional \$8 million over the President's budget of \$19 million. This provides a total of \$27 million. This increase is needed to control such diseases as measles, rubella, polio, mumps, diphtheria, and tetanus. It would also allow an increased capability for targeted immunization programs to stem increases in diseases in disease outbreaks. For venereal disease, the AMA recommends a \$10 million increase over the \$18 million requested by the President for a total amount of \$28 million. This increase would allow an accelerated effort to stem the incidence of these highly communicable diseases which are now at unacceptable high levels.

*Lead Based Paint Poisoning in Children* — The AMA recommends an increase of \$2.5 million to the President's request of \$8.5 million. This would provide a total of \$11 million. This increase would allow additional assistance to communities in developing child screening and follow-up programs.

*Occupational Health* — We suggest an additional \$7 million over the President's request of \$49,177,000. This provides a total of \$56,177,000 and this additional amount would provide funds for basic research efforts to assure healthful and safe working conditions.

*Mental Health* — The AMA believes that the President's request of \$454,049,000 should be increased by \$60 million to a total of \$514,049,000. This additional amount would give the National Institute of Mental Health an increased capability in its work with the states and local communities to prevent and treat

mental disorders. We are pleased with the high priority the President has placed on this area of health care.

*Alcoholism* — The President's request of \$154,066,000 should be increased by \$30 million to \$184,066,000. This additional amount would allow the National Institute of Alcohol Abuse and Alcoholism to carry out a national program aimed at accumulating and disseminating knowledge to increase the level of awareness regarding the risks and dangers associated with irresponsible drinking and to increase the capacity of the states and local communities to establish and sustain programs of prevention, treatment and rehabilitation.

*Health Professions Education* — The AMA recommends an increase of \$180 million to the President's request of \$544,619,000. This would provide a total of \$724,619,000. By increasing the funds for health professions schools and student financing, health care can be made increasingly available to all segments of the population. It would assist in alleviating the maldistribution of health professionals by increasing the available supply of primary care physicians and auxiliary health personnel.

*National Institutes of Health* — AMA recommends an increase of \$256 million to the President's request of \$2,567,371,000. This provides a total of \$2,823,371,000. This additional amount would allow increases for those institutes that have demonstrated progress in essential research into the cause and treatment of disease. The budget as proposed would be a step backward for necessary research in cancer, heart, lung, child health and human development, aging, dental, eye, and environmental health services.

*Programs for Older Americans* — AMA recommends an increase of \$70 million to the President's request of \$423,450,000. This provides a total budget of \$493,450,000. This additional amount would allow a continued emphasis on service programs that are aimed at securing and maintaining independence and dignity for older Americans and would improve care and services which can prevent or delay institutionalization of the physically and mentally impaired elderly.

*Food and Drug Administration* — The AMA recommends an increase of \$30 million to the President's request of \$279,258,000 for a total amount of \$309,258,000. This additional amount would allow the FDA to expand its activities to protect the health and safety of the public.

*Indian Health Service* — We urge that the President's request of \$442 million be increased by \$27



million to a total of \$469 million. This additional amount would allow for the recruiting, training and retention of skilled health professionals to provide improved health care for Indians. It would also permit the renovation and expansion of Indian Health Service facilities which do not meet adequate standards.

---

### PHYSICIANS' BUSINESS COSTS OUTPACING THEIR FEES, AMA SAYS

CHICAGO — Physicians' fees have been rising rapidly. But their fees have not been rising as rapidly as their business expenses. And physicians' incomes per patient visit have not risen as much as the cost of living.

Those conclusions are based on an analysis of physicians' fees for the years 1971-1975. (See attached table.)

During the first three years of that period, 1971-1974, physicians' fees rose substantially *less* rapidly than the overall cost of living, up about 5.1 percent a year for physicians' fees and 6.1 percent for the Consumer Price Index (all items). Then in 1975, physicians' fees went up by 12.3 percent while the CPI registered a 9.1 percent increase. In 1976, the annual average increases were: physicians' fees, 11.3 percent; CPI, 5.8 percent.

Why do physicians' fees rise as they do? To see why, it is helpful to divide physicians' fees (as measured by the CPI) into two main components — the portion that helps pay the wages of the doctor's staff, office rent, and other business expenses; and the portion the doctor pays himself.

During most of 1971-1974, increases in doctor fees were tightly curbed by government-imposed price controls. Doctors' business costs during that period went up about 18.5 percent, which was a faster climb than their fees, 16.3 percent.

Doctors' incomes per patient visit went up about 14.7 percent during that period, while the cost of living went up 21.8 percent. In effect, the purchasing power of physicians' earnings declined.

Price controls on physicians' fees were lifted in 1974. During the following year, 1975, physicians' business expenses (many of which could be anticipa-

ted at the beginning of the year) went up by 12.3 percent. The largest increase in doctors' business costs was malpractice insurance, which went up 84 percent.

It may be that many doctors simply increased their fees according to their business costs. Average increase in physicians' fees was the same as the increase in their business expenses, 12.3 percent. As a result, physicians' incomes per patient visit rose at nearly the same rate as their fees, 12.2 percent.

In effect, physicians in 1975 allowed themselves a partial cost of living increase.

While it is believed that a large portion of the 1976 increase in physicians' fees was attributable to increases in malpractice insurance rates, analysis will not be possible until the appropriate data become available.

(The foregoing analysis is summarized in the attached table. It indicates that: 1) physician fees have not risen as much as their expenses; and 2) physician income has not risen as much as the cost of living.)

### INDICES OF PHYSICIANS' FEES AND THE COST OF LIVING (1971 = 100)

	1974	1975
Physicians' Fees	116.3	130.5
Business expenses component	118.5	133.1
Physicians' income component	114.7	128.8
Cost of Living (CPI, all items)	121.8	132.9

---

#### SOURCES:

1. Physicians' fees and cost of living from the Consumer Price Index.

2. Business expense component from HEW data in Federal Register, June 16, 1975 (page 25502) and September 8, 1976 (page 37838).

3. Income component estimated from the above-listed CPI and Federal Register data.

---

### PHYSICIAN INCOMES SIMILAR TO EXECUTIVE

## SALARIES

CHICAGO — How do physicians' incomes compare with those of non-medical professionals?

Comparison with a 1974 government study indicates that the average physician's income falls at about the midrange of corporate executive salaries. The comparison is not exact, however.

The average physician netted \$51,224 (after business expenses) from his practice in 1974, according to the American Medical Association. His gross receipts totaled \$86,575 and his business expenses totaled \$35,351. (These are the AMA's latest published estimates.)

According to the *Statistical Abstract of the U. S.* (1976 edition), 1) median net earnings for a physician under age 65 in 1974 was \$44,580; and 2) median net earnings for physicians (all ages) in incorporated practices was \$61,500. (Some physicians incorporate their practices because of certain tax advantages.) Source of the *Statistical Abstract's* information was *Medical Economics*, a professional magazine.

In 1974, the U. S. Civil Service Commission surveyed the salaries of eight non-medical professional occupations at the middle-management and executive levels of 144 American companies. Corporate officers were generally not included in the government survey.

Results of the survey, with average physicians' income added for comparison, are shown on the two attached tables. As table I indicates the average physician's net income is generally greater than the average salaries of the eight non-medical professions.

Salaries among these professions varied, however, according to the individual's level of responsibility within the corporate structure. Table II summarizes the average salaries of the same eight professional groups according to their levels of responsibility.

Table II shows that physicians' incomes tend to be at the low side of the "C" level, mid-range among corporate executives, on the scale of corporate responsibility levels.

This comparison is far from exact, however. The reason: employees of most American companies receive certain "fringe" benefits — such as health and life insurance — in addition to their wages. Personnel people with whom we checked report that companies tend to pay out about 30 to 35 cents in fringes for every dollar of payroll.

Physicians, on the other hand, are typically self-employed individuals and, as such, do not receive

most such fringes in addition to their earnings. Rather, they must purchase most such benefits from their after-business-expense earnings. (An exception is a Kcogh-type retirement plan, in which the physician's contribution is tax-deductible).

If we assume that the equivalent of fringe benefits accounted for 15 percent to 25 percent of a physician's net income in 1974, his "take home pay" was around the \$38,000 to \$45,000 range. That is, his personal earnings were roughly equivalent to those of a senior manager or a junior executive (or somewhere between "D" and "E" on the Table II scale).

\* \* \*

How have incomes, both corporate and physician, changed since 1974? Precise figures are not available. However, a survey of executive pay in some 300 companies, conducted for the Commission on Executive, Legislative and Judicial Salaries, indicated an average salary increase of 6.2 percent per year during 1969-1976. Among companies where no bonuses were paid, executive salaries rose by 6.8 percent a year.

An analysis by the AMA of the physicians' fee index of the Consumer Price Index indicated that physicians' net income per patient visit rose by about 6.5 percent a year during 1971-1975.

Thus, it appears likely, assuming no major change in physicians' patient loads, that physician net incomes hold about the same relative position today, compared with other non-medical professional salaries, as they held in 1974.

TABLE I  
AVERAGE ANNUAL EARNINGS OF PHYSICIANS  
AND NON-MEDICAL PROFESSIONALS, 1974

	Manufacturing	Non-Manufacturing
Physicians*	----	\$51,224
Directors of Personnel	\$38,476	33,941
Attorneys	35,319	36,510
Chief Accountants	32,665	32,970
Engineers	33,500	32,903
EDP Program Mgrs.	34,102	37,039
Plant Managers	32,892	41,655
Commercial Mgrs.	25,987	32,100
Economists	39,657	33,943
AVERAGE, non-medical professions	\$34,055	\$33,515

\*AMA estimate

Source: "Study of Private Enterprise Pay Rates for Positions Equivalent to GS-14/18," U.S. Civil Service Commission, June 1974.

TABLE II

AVERAGE ANNUAL EARNINGS OF PHYSICIANS AND NON-MEDICAL PROFESSIONALS, BY LEVEL OF CORPORATE RESPONSIBILITY, 1974

	Manufacturing	Non-Manufacturing
Physicians *	----	\$51,224
Executive Levels **		
B	\$68,725	76,720
C	52,693	57,824
D	44,226	45,892

Middle Management Levels \*\*

E	35,490	36,797
F	29,224	28,013

AVERAGE, non-medical professions \$34,055 \$33,515

\* AMA estimate

\*\* "B" is just at or below the level of corporate officer. The "A" level, corporate officer, was generally not included in the survey. "D" is the lowest executive level.

Source: "Study of Private Enterprise Pay Rates for Positions Equivalent to GS-14/18," U. S. Civil Service Commission, June 1974.

## A N U N C I O S

### URBANIZACION SAN FRANCISCO RIO PIEDRAS

Atractiva residencia propia para oficina médico y/o laboratorios, próxima a centro comercial y colegios Santa María Reina y San Ignacio. Solar 1551.85 m<sup>2</sup>, 4,251 pies cuadrados de sólida construcción, 3 niveles, pisos terrazo integral, 5 dormitorios, 5 1/2 baños, habitación de servicio con baño, terraza galería, cocina equipada, aire central en las habitaciones, biblioteca, piscina, verja, rejas y sobre todo una localización

ñas, teléfonos 723-6796 y 722-6874 o Metropolitan Real Estate — teléfonos 790-1072, 790-1073 y 789-3736.

### SE ALQUILA LOCAL A MEDICO

Lugar de mucho tráfico, en Avenida Barbosa 330, Hato Rey, Puerto Rico. Agua y luz incluida en la renta — \$300.00. Información: Sr. Colón Cuevas, teléfonos 767-1366 y 763-0941.



## LISTA DE ANUNCIANTES

- |                        |                 |
|------------------------|-----------------|
| 1. BELTONE ELECTRONICS | HEARING AIDS    |
| 2. CIBA PHARM.         | VIOFORM - HC    |
| 3. EATON LAB.          | MACRODANTIN     |
| 4. PENNWALT CORP.      | ZAROXOLYN       |
| 5. ROCHE LAB.          | LIBRIUM, VALIUM |
| 6. RORER INTERNATIONAL | MAALOX PLUS     |
| 7. UPJOHN COMPANY      | MEDROL DOSEPAK  |
| 8. U. S. V. PHARM.     | REGROTON        |

\*\*\*\*\*



There is only one  
macrocrystal  
nitrofurantoin...  
and only Eaton  
has it.

Eaton

Consistent  
potency  
against the  
most prevalent  
uropathogens.

# Macrochantin<sup>®</sup> (nitrofurantoin macrocrystals)

capsules 25mg 50mg 100mg



<sup>®</sup> EATON LABORATORIES

Norwich International  
410 Park Avenue  
New York, N.Y. 10022  
U.S.A.

**INDICATIONS:** Indicated for the treatment of pyelonephritis, pyelitis, and cystitis due to susceptible *E. coli*, enterococci, *S. aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses) and certain strains of *Klebsiella-Aerobacter*, *Proteus* and *Pseudomonas*.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function, infants under one month; pregnant patients at term; known hypersensitivity.

**WARNINGS:** May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. (Such patients should be closely observed while receiving nitrofurantoin.) Discontinue the drug at any sign of hemolysis.

Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to *Pseudomonas*. Safety not established during pregnancy and lactation, should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.

**PRECAUTIONS:** Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal

impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**ADVERSE REACTIONS: Gastrointestinal Reactions**—Anorexia, nausea, emesis are the most frequent reactions, less frequently, abdominal pain and diarrhea, rarely, hepatitis. This dose-related toxicity reaction can be minimized by reduction of dosage, especially in the female patient.

**Hypersensitivity Reactions**—Pulmonary sensitivity reactions, which can be acute, subacute, or chronic. Acute reaction is commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on X-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and resolve with cessation of the drug therapy. Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation

of the drug therapy.

**Dermatologic Reactions**—Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other Sensitivity Reactions**—Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and orthralgia.

**Hematologic Reactions**—Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurological Reactions**—Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

**Miscellaneous Reactions**—Transient alopecia.

**SUPPLIED:** Macrochantin (nitrofurantoin macrocrystals) is available in opaque, yellow capsules of 100 mg (coded "Eaton 009") and in opaque, yellow and white capsules of 50 mg (coded "Eaton 008") in bottles of 30, 100, 500, and 1,000 capsules, and in opaque, white capsules of 25 mg (coded "Eaton 007") in bottles of 100 capsules. Macrochantin Capsules, 50 mg and 100 mg, are also available in hospital unit-dose packages, strip-packaged in boxes of 100



#### Brief Summary

**Indication:** Hypertension. (See box warning.)

**Contraindications:** Mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.

#### Warnings:

This fixed combination drug is not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Use with caution in patients with severe renal disease, impaired hepatic function or progressive liver disease. Regroton may potentiate action of other antihypertensive, ganglionic and peripheral adrenergic-blocking drugs. Sensitivity reactions may occur in allergic and asthmatic patients. Discontinue Regroton one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Thiazides cross the placental barrier and appear in cord blood. The use of chlorthalidone and related drugs in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Use with care in nursing mothers since thiazides and reserpine cross the placental barrier and appear in cord blood and breast milk. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated mothers. If use of the drug is essential, the patient should stop nursing.

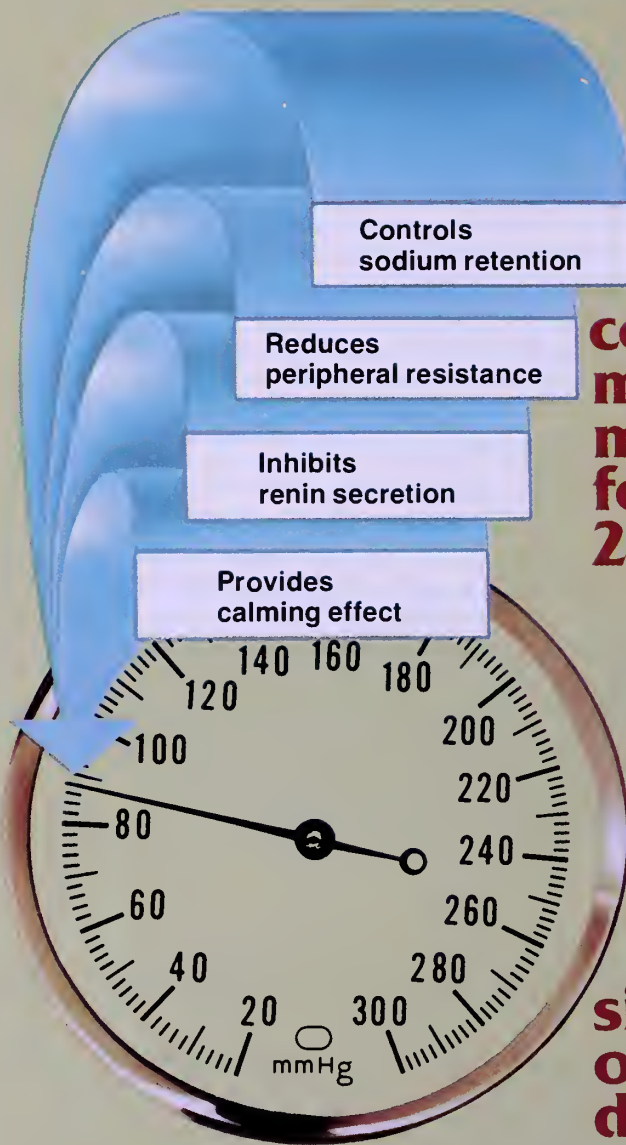
**Precautions:** Antihypertensive therapy with this drug should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with this agent two weeks prior to elective surgical procedures. In emergency surgery, use anticholinergic or adrenergic drugs or other supportive measures if needed. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue Regroton if the BUN rises or liver dysfunction is aggravated (hepatic coma may be precipitated). Patients receiving chlorthalidone should have periodic determination of serum electrolytes and should be observed for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis and hypokalemia), particularly if they are receiving digitalis, parenteral fluids, or are vomiting excessively. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. Use Regroton cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients.

**Adverse Reactions:** The drug is generally well tolerated. The most frequent adverse reactions are anorexia, nausea, vomiting, gastric irritation, diarrhea, constipation, headache, dizziness, weakness, muscle cramps, nasal congestion, drowsiness and mental depression. Other potential side effects include skin rash, urticaria, ecchymosis; hyperglycemia and glycosuria (diabetics should be checked regularly), hyperuricemia and acute gout, and impotence. With chlorthalidone: restlessness, transient myopia, dysuria, orthostatic hypotension (may be potentiated by alcohol, barbiturates or narcotics), rare idiosyncratic reactions such as aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, purpura, necrotizing angitis and Lyell's syndrome (toxic epidermal necrolysis); pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration; other reactions reported with this class of compounds include jaundice, xanthopsia, paresthesia, and photosensitization. With reserpine: angina pectoris, bradycardia, ectopic cardiac rhythms (especially with digitalis); blurred vision, conjunctival injection, uveitis, optic atrophy, glaucoma, deafness, increased gastric secretions, dull sensorium, paradoxical anxiety, nightmares, reversible paralysis agitans syndrome, dyspnea, weight gain, dryness of mouth, increased susceptibility to colds, decreased libido, skin flushing and pruritus. **Dosage:** Should be determined by individual titration. (See box warning.) Dosage for most patients is one tablet once a day.

**How Supplied:** Pink, round, single-scored tablets in bottles of 100 and 1000.

# In moderate to moderately severe hypertension

## Regroton®



Combines two long-acting agents... following titration, offers a simple regimen that encourages compliance through convenience and economy.

# Regroton®

Each tablet provides:  
chlorthalidone USP 50 mg., reserpine USP 0.25 mg.

## matches medication to mechanisms

**USV**  
LABORATORIES

USV Laboratories Inc.  
Manati, P.R. 00701



# Just what do you get for your AMA dues?

You get a package of personal and professional benefits and services that are the most extensive of any professional organization.

You get group insurance programs that provide coverage at far lower costs than individual coverage. They include: Group Life Insurance, Excess Major Medical, Disability Income Insurance, Supplemental "In Hospital" Insurance, Accidental Death and Dismemberment Plan, and Office Overhead Insurance.

You get publications to keep you abreast of medical and health developments: *JAMA*,

*American Medical News*, and one of nine specialty journals.

There's the AMA Members Retirement Plan. Professional practice management information and guides. Authoritative legal information. Continuing medical education. The nation's largest physician placement service. The research resources of one of the nation's greatest medical libraries.

These are just a few of the broad range of benefits you get for your dues. Even more important, you get a strong and effective spokesman to represent you, your interests, and your views.



**Join us.  
We can do much more together.**

Dept. of Membership Development  
American Medical Association  
535 N. Dearborn St./Chicago, IL 60610

Please send me more information on the AMA and AMA membership.

Name \_\_\_\_\_

Address \_\_\_\_\_

City/State/Zip \_\_\_\_\_

Great taste  
means better  
compliance

**Maalox<sup>®</sup>**  
**Plus** MAGNESIUM  
& ALUMINUM  
HYDROXIDES  
plus  
**SIMETHICONE**  
LEMON SWISS CREME FLAVOR

The best  
tasting antacid  
you can  
recommend



WILLIAM H. RORER, INC.  
Fort Washington, Pa. 19034



# ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES

SEP 14 1977

**BOLETIN**

THE FRANCIS A. COMPTON  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET



**VOL. 69**

**Julio**

**1977**

**No.7**



# A character all its own.



Valium (diazepam) is a benzodiazepine with a character all its own.

Pharmacologically, it has been described as more potent mg-per-mg than other available anxiolytic benzodiazepines. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> (diazepam)<sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

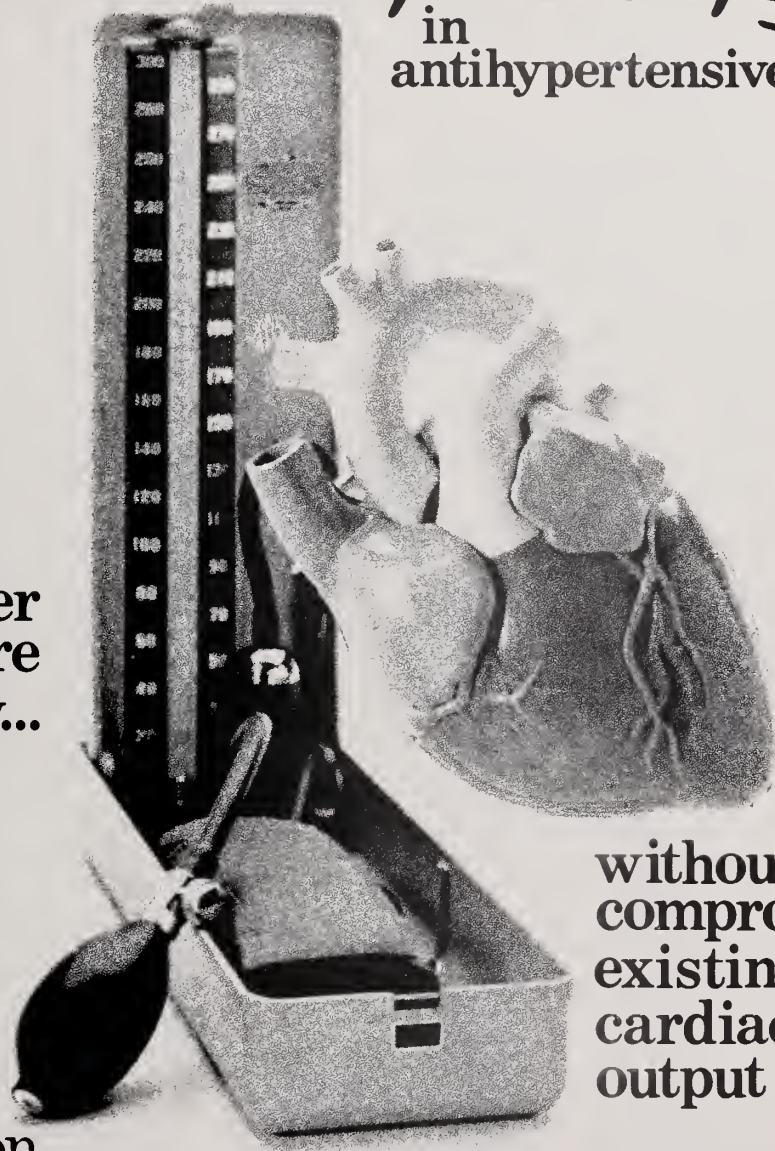
ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

# A Dual Challenge

in  
antihypertensive therapy

to lower  
blood pressure  
effectively...



without  
compromising  
existing  
cardiac  
output

in hypertension

TABLETS: 250 mg, 500 mg, and 125 mg

# ALDOMET<sup>®</sup> (METHYLDOPA | MSD)

helps lower blood pressure effectively...  
usually with no direct effect on  
cardiac function—cardiac output  
is usually maintained

ALDOMET is contraindicated in active hepatic disease, hypersensitivity to the drug, and if previous methyldopa therapy has been associated with liver disorders. It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. For more details see the brief summary of prescribing information.

For a brief summary of prescribing information, please see following page.

**MSD**  
MERCK  
SHARP  
DOHME



in hypertension

# ALDOMET<sup>®</sup>

(METHYLDOPA|MSD)

helps lower  
blood pressure  
effectively...  
usually with no  
direct effect on  
cardiac function—  
cardiac output is  
usually maintained



**Contraindications:** Active hepatic disease, such as acute hepatitis and active cirrhosis; if previous methyldopa therapy has been associated with liver disorders (see Warnings); hypersensitivity

**Warnings:** It is important to recognize that a positive Coombs test, hemolytic anemia, and liver disorders may occur with methyldopa therapy. The rare occurrences of hemolytic anemia or liver disorders could lead to potentially fatal complications unless properly recognized and managed. Read this section carefully to understand these reactions.

With prolonged methyldopa therapy, 10% to 20% of patients develop a positive direct Coombs test, usually between 6 and 12 months of therapy. Lowest incidence is at daily dosage of 1 g or less. This on rare occasions may be associated with hemolytic anemia, which could lead to potentially fatal complications. One cannot predict which patients with a positive direct Coombs test may develop hemolytic anemia. Prior existence or development of a positive direct Coombs test is not in itself a contraindication to use of methyldopa. If a positive Coombs test develops during methyldopa therapy, determine whether hemolytic anemia exists and whether the positive Coombs test may be a problem. For example, in addition to a positive direct Coombs test there is less often a positive indirect Coombs test which may interfere with cross matching of blood.

At the start of methyldopa therapy, it is desirable to do a blood count (hematocrit, hemoglobin, or red cell count) for a baseline or to establish whether there is anemia. Periodic blood counts should be done during therapy to detect hemolytic anemia. It may be useful to do a direct Coombs test before therapy and at 6 and 12 months after the start of therapy. If Coombs-positive hemolytic anemia occurs, the cause may be methyldopa and the drug should be discontinued. Usually the anemia remits promptly. If not, corticosteroids may be given and other causes of anemia should be considered. If the hemolytic anemia is related to methyldopa, the drug should not be reinstituted. When methyldopa causes Coombs positivity alone or with hemolytic anemia, the red cell is usually coated with gamma globulin of the IgG (gamma G) class only. The positive Coombs test may not revert to normal until weeks to months after methyldopa is stopped.

Should the need for transfusion arise in a patient receiving methyldopa, both a direct and an indirect Coombs test should be performed on his blood. In the absence of hemolytic anemia, usually only the direct Coombs test will be positive. A positive direct Coombs test alone will not interfere with typing or

cross matching. If the indirect Coombs test is also positive, problems may arise in the major cross match and the assistance of a hematologist or transfusion expert will be needed.

Fever has occurred within first 3 weeks of therapy, sometimes with eosinophilia or abnormalities in liver function tests, such as serum alkaline phosphatase, serum transaminases (SGOT, SGPT), bilirubin, cephalin cholesterol flocculation, prothrombin time, and bromsulphalein retention. Jaundice, with or without fever, may occur, with onset usually in the first 2 to 3 months of therapy. In some patients the findings are consistent with those of cholestasis. Rarely fatal hepatic necrosis has been reported. These hepatic changes may represent hypersensitivity reactions; periodic determination of hepatic function should be done particularly during the first 6 to 12 weeks of therapy or whenever an unexplained fever occurs. If fever and abnormalities in liver function tests or jaundice appear, stop therapy with methyldopa. If caused by methyldopa, the temperature and abnormalities in liver function characteristically have reverted to normal when the drug was discontinued. Methyldopa should not be reinstituted in such patients.

Rarely, a reversible reduction of the white blood cell count with primary effect on granulocytes has been seen. Reversible thrombocytopenia has occurred rarely. When used with other antihypertensive drugs, potentiation of antihypertensive effect may occur. Patients should be followed carefully to detect side reactions or unusual manifestations of drug idiosyncrasy.

**Use in Pregnancy:** Use of any drug in women who are or may become pregnant requires that anticipated benefits be weighed against possible risks; possibility of fetal injury can not be excluded.

**Precautions:** Should be used with caution in patients with history of previous liver disease or dysfunction (see Warnings). May interfere with measurement of: uric acid by the phosphotungstate method, creatinine by the alkaline picrate method, and SGOT by colorimetric methods. Since methyldopa causes fluorescence in urine samples at the same wavelengths as catecholamines, falsely high levels of urinary catecholamines may be reported. This will interfere with the diagnosis of pheochromocytoma. It is important to recognize this phenomenon before a patient with a possible pheochromocytoma is subjected to surgery. Methyldopa is not recommended for patients with pheochromocytoma. Urine exposed to air after voiding may darken because of breakdown of methyldopa or its metabolites.

Stop drug if involuntary choreoathetotic movements occur in patients with severe bilateral cerebrovascular disease. Patients may require reduced doses of anesthetics; hypotension occurring during anesthesia usually can be controlled with vasopressors. Hypertension has recurred after dialysis in patients on methyldopa because the drug is removed by this procedure.

**Adverse Reactions:** *Central nervous system:* Sedation, headache, asthenia or weakness, usually early and transient; dizziness, lightheadedness, symptoms of cerebrovascular insufficiency, paresthesias, parkinsonism, Bell's palsy, decreased mental acuity, involuntary choreoathetotic movements; psychic disturbances, including nightmares and reversible mild psychoses or depression.

*Cardiovascular:* Bradycardia, aggravation of angina pectoris. Orthostatic hypotension (decrease daily dosage). Edema (and weight gain) usually relieved by use of a diuretic. (Discontinue methyldopa if edema progresses or signs of heart failure appear.)

*Gastrointestinal:* Nausea, vomiting, distention, constipation, flatulence, diarrhea, mild dryness of mouth, sore or "black" tongue, pancreatitis, sialadenitis.

*Hepatic:* Abnormal liver function tests, jaundice, liver disorders.

*Hematologic:* Positive Coombs test, hemolytic anemia. Leukopenia, granulocytopenia, thrombocytopenia.

*Allergic:* Drug-related fever, myocarditis.

*Other:* Nasal stuffiness, rise in BUN, breast enlargement, gynecomastia, lactation, impotence, decreased libido, dermatologic reactions including eczema and lichenoid eruptions, mild arthralgia, myalgia.

**Note:** Initial adult dosage should be limited to 500 mg daily when given with antihypertensives other than thiazides. Tolerance may occur, usually between second and third month of therapy; increased dosage or adding a thiazide frequently restores effective control. Patients with impaired renal function may respond to smaller doses. Syncope in older patients may be related to increased sensitivity and advanced arteriosclerotic vascular disease; this may be avoided by lower doses.

**How Supplied:** Tablets, containing 125 mg methyldopa each, in bottles of 100; Tablets, containing 250 mg methyldopa each, in single-unit packages of 100 and bottles of 100 and 1000; Tablets, containing 500 mg methyldopa each, in single-unit packages of 100 and bottles of 100.

**For more detailed information, consult your MSD representative or see full prescribing information. Merck Sharp & Dohme, Division of Merck & Co., Inc., West Point, Pa. 19486 J6AM07 (707)**

**MSD** MERCK SHARP & DOHME



# *Lifesaving Partnership... Against Cancer Quackery*

The anguish associated with cancer is compounded by the cancer quack. False hopes—harmful delays—devastating expenses—deceptive diagnoses—loss of life—these are hazards facing the cancer patient desperate enough to seek a cancer quack.

*The problem:* how to divert the patient from this tragic encounter.

As medical guide, family counselor, trusted friend—you, *doctor*, play a major role in the fight against cancer quackery.

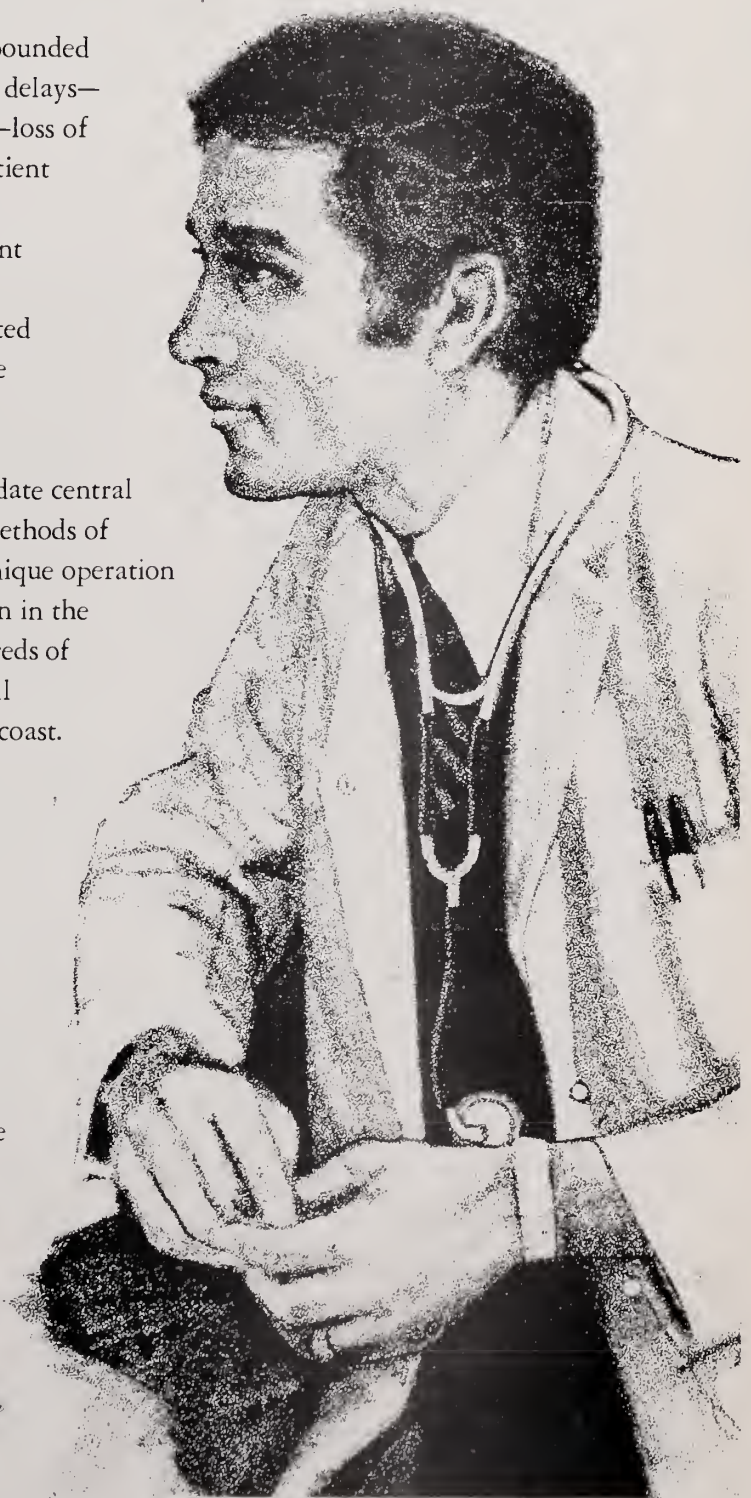
We are here to serve as your partner.

Our National Office maintains an up-to-date central clearinghouse for materials on unproven methods of cancer diagnosis and treatment. This is a unique operation and the principal source of such information in the country. Its services are widely used. Hundreds of inquiries are received and answered from all segments of the community, from coast to coast.

To trigger grass-roots action, we have formulated a model State Cancer Remedy Act designed to control the promotion and sale of unproven methods of cancer management. This has helped to inspire some 20 states to enact or consider legislation against cancer quackery—with active support from the medical community. Copies of the model act, as well as copies of laws in effect, are available through our National and Division offices.

In these actions against cancer quackery, as in all our efforts against cancer, ours is a lifesaving partnership.

*American Cancer Society* ✽



# ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial

Fundado en 1903

Volumen 69

Julio 1977

Número 7

## JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bermúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

## Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

## Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

## Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Comparative Study of Amikacin (BB-K8 and Gentamicin Activity In Vitro against <i>Proteus Rettgeri</i> .....	222
Felipe Pérez Rodríguez, MD, Ramón H. Bermúdez, MD, FACP and Carmen Javier de Brau, MT	
Artificial Insemination Donor .....	227
Walter M. Pinedo, MD, FACOG and Rafael Rodríguez Acevedo, MD	
Commentary: Conservative Treatment of Splenic Injuries in Children .....	233
Pedro J. Rosselló, MD	
Las Pruebas Cutáneas y la Alergia a Penicilina.....	237
Carlos F. León Valiente, MD y Carlos H. Ramírez Ronda, MD, FACP	
Nuevos Conceptos en la Patofisiología de Hipertensión.....	241
José L. Cangiano, MD	
Noticias .....	246

PORTADA: CENTRO DE ARTES POPULARES  
VIEJO SAN JUAN  
(Cortesía - Rafael Tacoronte)

## COMPARATIVE STUDY OF AMIKACIN (BB-K8) AND GENTAMICIN ACTIVITY IN VITRO AGAINST *PROTEUS RETTGERI*

Felipe Pérez-Rodríguez, MD, Ramón H. Bermúdez, MD, FACP and  
Carmen Javier de Brau, MT

**Abstract:** Susceptibility of 28 urinary strains of *Proteus rettgeri* to Amikacin and Gentamicin in vitro was studied using concentrations of the antibiotics ranging from 0.15 to 80 mcg/ml and from 0.9 to 50 mcg/ml, respectively. An inoculum of approximately  $10^5$  organisms was used and a standard twofold serial dilution technique in trypticase soy broth was followed. Sensitivity was also tested by the Kirby-Bauer disc method in Mueller-Hinton agar plates. The organisms were isolated from the urine of patients from the Veterans Administration Center and from the Puerto Rico Medical Center at San Juan, Puerto Rico. Eleven of 28 (39 percent) strains were resistant to Gentamicin and only one of the 28 (3 percent) to Amikacin by the disc method. Six of the 28 (21 percent) were resistant to 20 mcg/ml of Amikacin and twenty-one of them (75 percent) were resistant to 10 mcg/ml. Nine of the 28 (32 percent) were resistant to 25 mcg/ml of Gentamicin and fifteen (54 percent) of these were resistant to 12.5 mcg/ml. Previous reports have shown that serum concentrations of 20 mcg/ml of Amikacin or 8 mcg/ml of Gentamicin are bactericidal for the organisms studied.

In general, the organisms obtained from

the Medical Center were more sensitive than the ones from the VA Center and there were more sensitive strains to Amikacin than to Gentamicin.

Amikacin may be the drug of choice in the treatment of severe infections with multiple antibiotic-resistant strains of *Proteus rettgeri*.

**Resumen:** La susceptibilidad "in vitro" de 28 cepas de *Proteus rettgeri* obtenido en urocultivos fue estudiada utilizando concentraciones que fluctuaban desde 0.15 a 80 mcg/ml de Amikacina y de 0.9 a 50 mcg/ml de Gentamicina, respectivamente. Las cepas de bacterias estudiadas fueron aisladas de cultivos de orina de pacientes de la Administración de Veteranos y del Centro Médico en San Juan, Puerto Rico. El inóculo consistió de aproximadamente  $10^5$  organismos/ml. Diluciones seriadas fueron hechas en caldo de tripticasa soya. Pruebas de susceptibilidad utilizando el método de Kirby-Bauer fueron hechas simultáneamente.

Utilizando el método de Kirby-Bauer, 11 de las 28 cepas (39 por ciento) demostraron resistencia a Gentamicina y 1 de las 28 cepas (3 por ciento) demostraron resistencia a Amikacina. Utilizando el método de dilución, 6 de las 28 cepas (21 por ciento) fueron resistentes a 20 mcg/ml de Amikacina y 21 de las 28 (75 por ciento) fueron resistentes a 10 mcg/ml de Amikacina. Nueve de las 28 cepas (32 por ciento) fueron resistentes a 25 mcg/ml de Gentamicina, 15 de las 28 cepas (54 por ciento) fueron resistentes a concentración de 12.5 mcg/ml de

---

From the Infectious Disease Section, Departments of Medicine and Research, Veterans Administration Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.

Request reprints to: Ramón H. Bermúdez, MD, Infectious Disease Section, Veterans Administration Hospital, GPO Box 4867, San Juan, Puerto Rico 00936.



## Gentamicina.

Reportes anteriores indican que las concentraciones bactericidas para estos organismos son 20 mcg/ml de Amikacina y 8 mcg/ml de Gentamicina. En general, las cepas provenientes de pacientes del Centro Médico fueron más susceptibles que las bacterias aisladas de pacientes de la Administración de Veteranos y en general mostraron mayor susceptibilidad a Amikacina que a Gentamicina. Amikacina puede ser la droga a usarse en el tratamiento de infecciones severas por cepas de *Proteus rettgeri* resistentes a múltiples antibióticos.

Gram-negative bacterial infections have become an increasingly serious problem among hospitalized patients. Several reports have been recently published regarding infections due to hospital-acquired strains of *Proteus rettgeri* resistant to multiple antibiotics (1, 2). We were encountering similar difficulties with *Proteus rettgeri*-resistant strains and this finding prompted us to study Amikacin.

Amikacin (BB-K8) is a new semisynthetic aminoglycoside antibiotic with pharmacological properties similar to those of Kanamycin, but, with a broader antibacterial spectrum which includes pseudomonads and Kanamycin-resistant strains of staphylococcus and enterobacteriaceae (3, 4, 5).

The following report summarizes a study in which the susceptibility of several strains of *Proteus rettgeri* to Amikacin and Gentamicin in vitro was compared.

## Materials and Methods

*Proteus rettgeri* was isolated from the urine of patients from two different centers: Veterans Administration Center and the Puerto Rico Medical Center at San Juan, Puerto Rico. The organisms were cultured, maintained in CTA media and subcultured every two or three weeks. Trypticase soy broth (TSB) was inoculated with a wire loop from each specimen and these were

incubated overnight. A 1:1000 dilution with broth was prepared from each of these cultures to obtain a solution containing approximately  $10^5$  organisms/ml.

Gentamicin and Amikacin solutions were prepared and the standard twofold serial dilution method was followed from 50 to 0.9 and from 80 to 0.15 mcg/ml respectively. All tubes were inoculated with 0.5 ml, the solution containing approximately  $10^5$  organisms/ml and were incubated overnight in tubes containing 0.5 ml of Trypticase soy broth (TSB).

The minimal inhibitory concentration (MIC) was determined as the lowest concentration of antibiotic where no growth was visually observed. The minimal bactericidal concentration (MBC) was considered as the lowest concentration of antibiotic where there was no growth after subcultures in blood agar plates.

Sensitivity of all organisms was also tested by the Kirby-Bauer disc method in Mueller-Hinton agar plates (6). An inhibition zone of 13 mm or more for Gentamicin and of 13 mm or more for Amikacin was indicative of sensitivity to the antibiotic.

Gentamicin discs and powder were supplied by Schering Laboratories, Union, New Jersey. Amikacin discs and powder were supplied by Bristol Laboratories, Syracuse, New York.

## Results

The results are summarized in Tables 1 and 2. The MIC for Amikacin was between 10 and 20 mcg/ml and for Gentamicin between 12.5 and 25 mcg/ml. The MBC for Amikacin was 40 mcg/ml and for Gentamicin was 25 mcg/ml.

Eleven of 28 (39 percent) strains were resistant to Gentamicin and only one (3 percent) to Amikacin by the Kirby Bauer disc method.

Twenty-two of 28 (79 percent) strains had an MIC of 20 mcg/ml or less for Amikacin; of these, seven were sensitive to 10 mcg/ml. Nineteen of the 28 (68 percent) strains were sensitive to 25 mcg/ml of Gentamicin and of these, thirteen were sensitive to 12.5 mcg/ml or less.

Figures 1 and 2 show the relation between the zone of inhibition by the disc method and the MIC by the tube dilution me-

	Tube Dilution Method MIC of Amikacin in mcg/ml					Disc Method (Zone Size)	
	40	20	10	5	less than 5	13 mm or more	less than 13
Number of Specimens	6	15	5	2	0	27	1

Table I: Sensitivity of *Proteus rettgeri* to Amikacin

	Tube Dilution Method MIC of Gentamicin in mcg/ml						Disc Method (Zone Size)	
	50 or more	25	12.5	6.25	3.1	less than 3.1	13 mm or more	less than 13
Number of Specimens	9	6	9	3	1	0	17	11

Table II: Sensitivity of *Proteus rettgeri* to Gentamicin.

thod.

It is noted that correlation by the Kirby-Bauer and tube-dilution methods when Amikacin was tested was not clearly seen.

In general, it was noted that the strains obtained from the Medical Center were more sensitive to both antibiotics than the ones from the Veterans Administration Center.

### Discussion

Amikacin has been tested against different Gram-negative bacilli (1, 2, 7, 8). As *Proteus rettgeri* has become a frequently encountered pathogen of the urinary tract and it is resistant to many antibiotics, we wanted to test its sensitivity to Amikacin in our medical environment.

Previous studies have considered as sen-

sitive those organisms that were inhibited by a concentration of 20 mcg/ml of Amikacin or 8 mcg/ml of Gentamicin (2).

We found that of the 28 strains that we studied, twenty-seven were sensitive in vitro to Amikacin and seventeen to Gentamicin by the disc method. Twenty-two were sensitive to 20 mcg/ml or less of Amikacin and only thirteen were sensitive to 12.5 mcg/ml or less of Gentamicin. According to this finding 53 percent of the 28 strains were resistant to Gentamicin and 21 percent were resistant to Amikacin.

The *Proteus rettgeri* strains obtained at the VA Hospital were mostly from the paraplegic ward where these patients have indwelling catheters or are subject to repeated urinary catheterizations. The strains were usually resistant to Chloramphenicol, Kanamycin, Carbenicillin and

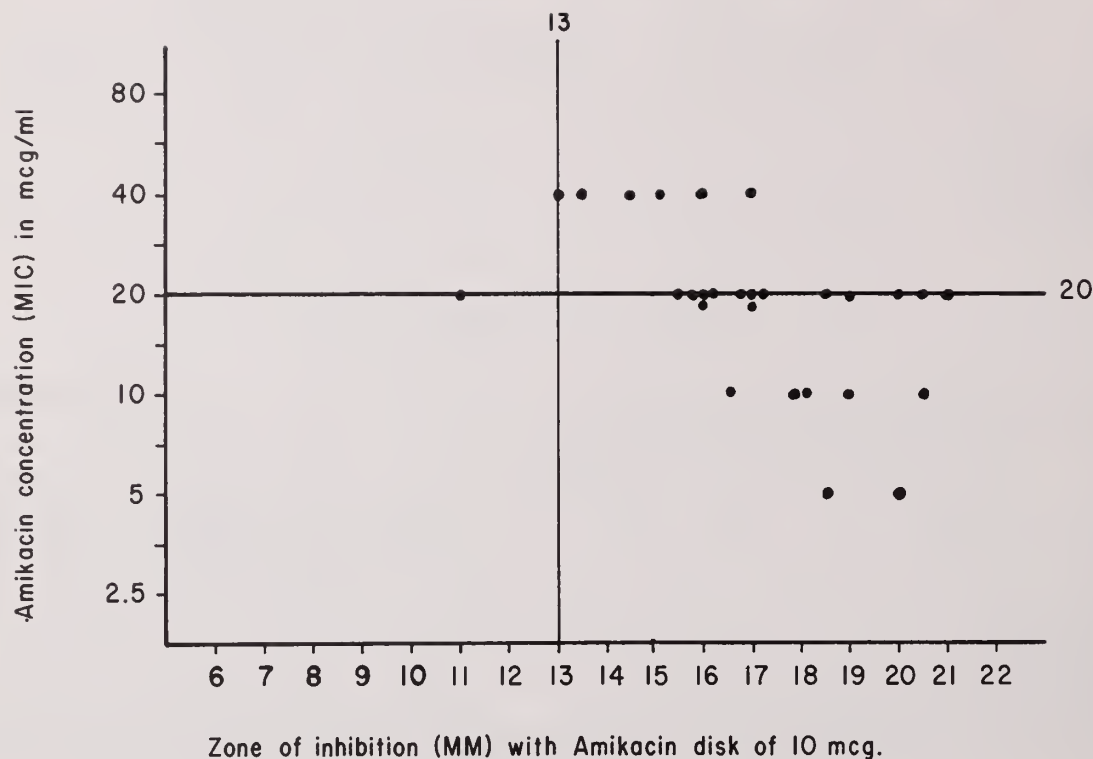


Fig. 1: Relation of zone sizes with MICs

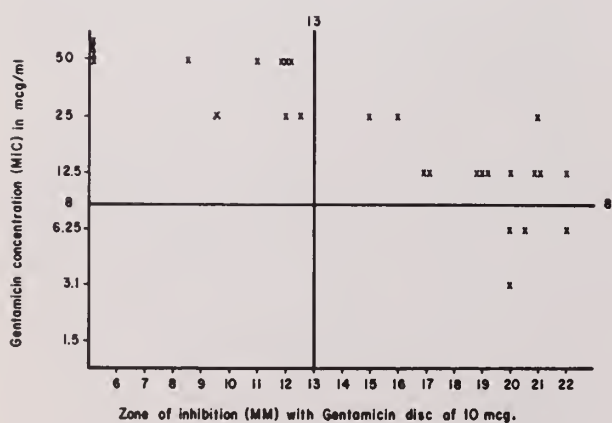


Fig. 2: Relation of zone sites with MICs

Polymyxin B. by the Kirby-Bauer disc method.

It has been shown that a dose of Amikacin of 300 mg/m<sup>2</sup> or 7.5 mg/kg intramuscular pro-

duces a high mean serum concentration of 25.4 mcg/ml with a mean serum concentration of 3.1 mcg/ml at 8 hrs and when administered at a dose of 150 mg/m<sup>2</sup> every six hours there was evidence of accumulation of the drug. Like Kanamycin most of the Amikacin is excreted in active form in the urine and the urinary levels of antibiotic are higher than in the serum (9).

We could not explain the disparity between the Kirby-Bauer and tube-dilution sensitivity methods when these antibiotics were tested (Tables 1, 2). This finding may be due to a more complete solubility of Amikacin in agar than Gentamicin, but this hypothesis was not tested.

In summary, we feel that Amikacin is an effective antibiotic for treating infections caused by *Proteus rettgeri* and that it may be safely used in clinical situations where significant Gen-



tamicin resistance is encountered with this particular organism. Our findings are consistent with recent clinical trials published by Tally, Bartlett, Gorbach and co-workers (10) regarding Amikacin therapy for severe Gram-negative sepsis with emphasis on infections with Gentamicin-resistant organisms.

### References

1. Sharp, P. M., Saenz, C. A. and Martin, R. R.: Amikacin (BB-K8) treatment of multiple drug resistant *Proteus* infection. *Antimicrob Ag Chemother* 5: 435-438, 1974.
2. Price, K. E., Pursiano, T. A., DeFuria, M. D. and Wright, G. E.: Activity of BB-K8 (Amikacin) against clinical isolates resistant to one or more aminoglycoside antibiotics. *Antimicrob Ag Chemother* 5: 143-152, 1974.
3. Bodey, G. P. and Stewart, D.: In vitro studies of BB-K8, a new aminoglycoside antibiotic. *Antimicrob Ag Chemother* 4: 186-192, 1973.
4. Kawaguchi, H., Naito, T., Nakagawa, S. and Fujisawa, K.: BB-K8 a new semisynthetic aminoglycoside antibiotic. *J Antibiot* 25: 695-708, 1972.
5. Price, K. E., Chisholm, D. R., Misick, M., Leither, S. and Tsai, Y. H.: Microbiological evaluation of BB-K8, a new semi-synthetic aminoglycoside. *J Antibiot* 25: 709-731, 1972.
6. Garrod, L. P. and Waterworth, P. M.: Tests of bacterial sensitivity to drugs. In H. F. Dowling (ed), *Disease of the Month. Year Book Medical Publishers, Chicago*, 1971, P 3-48.
7. Karney, W., Holmes, K. K. and Turck, M.: Comparison of five aminocyclitol antibiotics in vitro against *Enterobacteriaceae* and *Pseudomonas*. *Antimicrob Ag Chemother* 3: 338-342, 1973.
8. Young, L. S. and Hewitt, W. L.: Activity of five aminoglycoside antibiotics in vitro against Gram-negative bacilli and *Staphylococcus aureus*. *Antimicrob Ag Chemother* 4: 617-625, 1973.
9. Bodey, G. P., Valdivieso, M., Feld, R. and Rodríguez, V.: Pharmacology of Amikacin in Humans. *Antimicrob Ag Chemother* 5: 508-512, 1974.
10. Tally, F. P., Louie, T. S., Weinstein, W. M. et al: Amikacin therapy for severe gram-negative sepsis. *Ann Intern Med* 83: 484-488, 1975.

## ARTIFICIAL INSEMINATION DONOR

Walter M. Pinedo, MD, FACOG and Rafael Rodríguez Acevedo, MD

The first record of the use of artificial insemination dates from the 14th century. However, recognition of the principle of A.I. is documented in the Hebraic Talmud in the first 30 years of the second century. John Hunter is recognized as the original practitioner of insemination in humans in 1799. In 1866, the first publication in the United States on this procedure was published by Marion Sims. All applications up to this date dealt almost exclusively with homologous (husband) insemination. Not until 1890 did Robert L. Dickinson, in the greatest of secrecy, start using A. I. D. in this country.

It has been estimated that 10,000 babies are born each year as a result of A. I. D. The procedure raises emotional, ethical, and legal questions. The husband may feel devaluated and his virility questioned. For obvious reasons, the physician must never do insemination without the consent of both husband and wife. Both must be strongly in favor of the procedure, and the stability of their marriage, as well as their emotional maturity, should be established by the physician. Three points are worth emphasizing to the couple:

1. Donor insemination does not guarantee pregnancy. The success rate is about 50 to 70 percent.
2. The couple should give some thought to their feelings, should the child be born with a congenital anomaly. This

will occur in perhaps 4-5 percent of all pregnancies, irrespective of whether it follows normal intercourse or insemination.

3. The procedure is covered by law in only a few states. It is a wise precaution for the physician to have the couple sign a consent form.

Artificial insemination is a private matter between the physician and the couple. Discussion with friends or relatives should be absolutely forbidden.

### *Indications for A. I. D.*

1. Husband who has, for whatever reason, total azoospermia (surgical sterilization), severe oligospermia or necropermia refractory to treatment.
2. There is a RH incompatibility, in which the husband is homozygous RH positive, and his wife has given birth to one or more hydropic fetuses. Here, a RH negative donor would be used.
3. The husband has proven gene errors that will produce abnormalities of reproduction.
4. The wife has been shown to have ag-

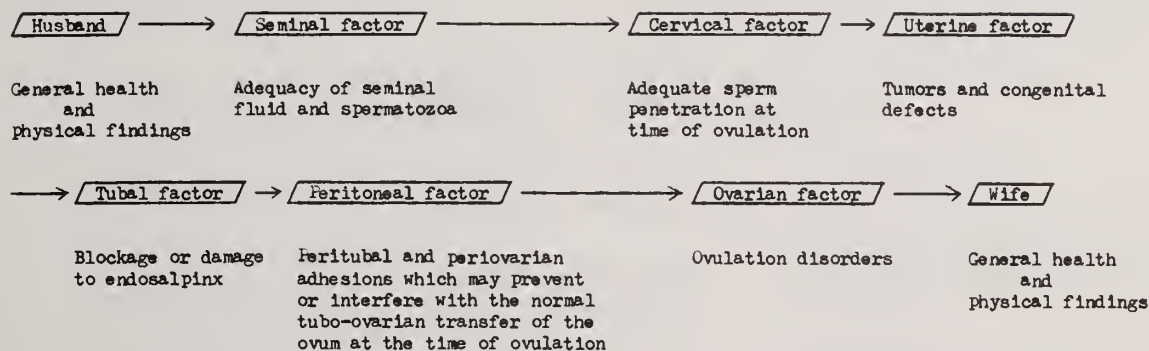


Fig. 1: Basic fertility factors to be investigated.

## STUDY OF THE FEMALE PARTNER

### Minimal Diagnostic Procedures:

1. History and physical examination.
2. Laboratory studies

#### Serology

Blood count and sedimentation rate

Urinalysis

3. T3 or T4.
4. Postcoital test.
5. Endometrial biopsy.
6. Tubal insufflation.
7. Miscellaneous

Papanicolaou's stain

Fern test – spinnbarkeit

Serial vaginal cytology

Hangingdrop for Candida and Trichomonas

Incompatibility test – cervical mucus and semen.

Figure 2

glutinating, but not immobilizing antibodies to her husband's semen.

### Fertility Work-Up

There is no indication for insemination on unmarried women, for whatever reason.

An infertility work-up is done for any infertile patient (Figure 1 and Figure 2). Special interest here, of course, is denoted to prove



# PROGESTERONE IN BLOOD

---

<i>January 1976 -</i>	<i>Progesterone 0.25 ng/ml (Follicular - No Ovulation).</i>
<i>February 1976 -</i>	<i>Progesterone 2.2 ng/ml (Follicular - No Ovulation).</i>
<i>March 1976 -</i>	<i>Progesterone 15 ng/ml (Luteal - OVULATION)</i>

## Normal Values:

<i>Female:</i>		<i>ng/ml.</i>
	<i>Prepubertal</i>	<i>0.10 - 0.34</i>
	<i>Follicular</i>	<i>0.20 - 0.90</i>
	<i>Luteal</i>	<i>3.0 - 36</i>
	<i>Postmenopausal</i>	<i>0.03 - 0.3</i>
	<i>Postmenopausal on contraceptive</i>	<i>0.2 - 0.5</i>
<i>Male:</i>		
	<i>Prepubertal</i>	<i>0.11 - 0.26</i>
	<i>Adult</i>	<i>0.12 - 0.31</i>

---

Figure 3

that the tubes are patent and to the timing of ovulation. We confirm tubal patency by hysterosalpingogram.

## The Donor

The donor should be unknown to the couple. His health and fertility must be unimpeachable and there should be no family history of genetic diseases. The donor will not be a mirror image of the husband, but an attempt should be made to match some physical characteristics, and his blood should be compatible with the A. B. O. and RH type of the recipient wife.

## Timing

The biggest single factor in unsuccessful insemination is the timing of ovulation. Pin-

pointing ovulation is often difficult in A. I., since the charged emotions of the patient can delay ovulation for a day or more. Different authors have recommended administration of estrogen I. V. or (human chorionic gonadotropin) H.C.G. I.M. in an effort to insure ovulation at the precise time.

Some of the adjuncts in helping to time ovulation are the B.B.T. chart, cervical mucus, vaginal cytology, and spinnbarkeit. Fuchs et al recommended the use of 5,000 to 10,000 I.U. of H.C. G. I.M. in the late follicular phase, to stimulate ovulation.

## Technique

We used Donor's Frozen Semen, collected and processed at Idant's New York laboratory.

1. There are many advantages to the use of frozen semen for anonymous donor insemination:

- a) Immediate and convenient access to semen from a diverse group of carefully screened donors of known genetic constitution. This eliminates the inconvenience of last minute calls to donors and the attendant difficulties of proper coordination with the ovulatory stage of the patient's menstrual cycle.
- b) Multiple inseminations in a given ovulatory cycle may be done, if desired, enhancing the probability of conception.
- c) Access to comprehensive and detailed information with regard to each semen specimen you use: blood type, RH factor, sperm count, motility, both before and after freezing, and the results of morphological examination of the spermatozoa of the donor.
- d) Tests of the donor's blood and semen for venereal disease and gonococcus are performed routinely, increasing the safety to the patient.
- e) A detailed profile of the donor is provided including, among other factors, genetic background, somatype, height, complexion, eye and hair color, education level, religion, etc.

2. The cost is comparable to the expense of obtaining fresh semen.

3. *Preparation*

Semen should be used within two or three minutes after its removal from the tank of liquid nitrogen. Therefore, the patient should be prepared for insemination before the frozen semen is withdrawn.

- a) Remove the top from the tank and locate the proper cane which contains the required insemination units.
- b) Lift the cane to the mouth of the tank and remove one straw (insemination unit) of semen. The straw may be removed from the cane with tweezers or directly with the fingers.
- c) It is not necessary for the semen to thaw prior to loading the inseminator.

4. *Loading the Inseminator*

- a) Unpack the inseminator and remove the metal plunger from the inseminator.
- b) Hold the straw level — horizontal — and cut the seal of each end of the straw. Do not hold the straw vertically, or the semen may run out.
- c) Holding the inseminator level — horizontal — slide the straw — white plug end *last* — into the inseminator (the end with the large rubber ring).
- d) Using the metal plunger, push the straw — *by the straw edge, not the plug* — down into the inseminator. The straw must slip over the cone end in the

inseminator tip.

- e) Still pressing the straw edge — *not the plug* — tap the straw several times to firmly seat the straw over the cone tip. If the straw is not tightly seated, the semen will leak out.
- f) Now slide the plunger past the straw end to the white plug. The inseminator is now ready for use.

#### 5. *Insemination Procedure Recommendations*

- a) Remove excess cervical mucus, if present, leaving a small amount in the cervical os.
- b) Insert inseminator about 1 cm into the cervical canal.
- c) Inseminate the woman daily, commencing two days prior to the anticipated date of ovulation, stopping on the day of ovulation.

#### Results

The best results reported in this category do not exceed 50 percent success within three or four months of exposure to the procedure. Almost 90 percent of the women, who will become pregnant, will do so within six months.

#### Case Presentation: R. M. M. No. 5910

Patient 28 years old: white female. Married nine years ago. No contraceptive. Never pregnant. Husband 42 years old; white male, vasectomy was done 10 years ago, five children in previous marriage. Two previous plastic surgeries, for recanalization of vas deferens, for having children, unsuccessfully.

Patient underwent complete infertility work-up with private M.D. in San Juan City, told to be O.K., and then referred for A. I. D.

Two A. I. D. were done on June 18, 1975 and July 31, 1975 at Farris Institute for Parenthood, Philadelphia, Pa. They used 50 mg Clomid daily for five days prior to each insemination. No pregnancy.

We saw this patient for the first time on August 28, 1975. Infertility work-up was done.

On September 29, 1975, we confirmed tubal patency by hysterosalpingogram and it was reported as normal.

On November 29, 1975 a biopsy of endometrium was taken as an indirect proof of ovulation and it was reported as proliferative endometrium (No ovulation).

On December 1975, we started with 50 mg Clomid daily for five days — begun on the 5th day of a cycle.

On January, Clomid was increased to 100 mg daily for five days, and on the 20th till the 22nd day of a cycle, blood was drawn for Progesterone in blood, as an indirect proof of ovulation, and corpus luteum formation and function. Progesterone in blood was reported as 0.25 ng/ml. (No ovulation).

On February, Clomid was given same dose and schedule, and Progesterone was reported to be 2.2 ng/ml. (No ovulation).

On March, Clomid was increased to 150 mg daily for five days, and Progesterone in blood was reported as 15 ng/ml. (*Ovulation*). (Figure 3).

Now, with proof of ovulation, we sent the request form for A. I. D. with frozen semen to Idant Corporation in New York.

L. M. P.: June 27, 1976, Clomid was given, 150 mg daily for five days — from July 2, 1976 till July 6, 1976 — then A. I. D. was performed on July 12-13-14, 1976. On July 12, the first day of A. I. D., we gave 5,000 I.U. H.C.G., intramuscular to insure ovulation at the precise time (Fuchs et al). The patient became pregnant, and was delivered by Cesarean section. She had a baby girl that weighed 8 lbs. 5 oz. The Apgar score was 8-9; The baby was examined by the pediatrician and was apparently normal.

#### Discussion

It is, therefore, clear that a large number of



infertile couples can be salvaged and given the satisfaction of raising their own children by either homologous or heterologous insemination, using fresh or frozen sperm. The two most important aspects of A. I. are a source of well-screened donors and the timing of insemination with ovulation. The use of frozen semen from banks offers great advantage when dealing with a subject as variable as a woman's ovulation. The results with frozen semen are not as good as those with fresh semen, and the offsprings have shown fewer anomalies than the general population — a fact that is encouraging, because of the concern about genetic damage to spermatozoos during the freezing process.

We present a case here that we believe to be the first A. I. D. with frozen semen in Puerto Rico.

## References

1. *Behrman, S. J.*: Artificial Insemination, in Progress In- fertility. Edited by SJ Behrman, RW Kistner. Boston, Little, Brown, 1975, p. 779.
2. *Behrman, S. J. and Sawada, J.*: Heterologous and homologous inseminations with human semen frozen and stored in a liquid-nitrogen refrigerator. *Fertil Steril* 17: 457, 1966.
3. *Beck, W. W.*: Artificial Insemination and Semen Preservation. *Clinical Obs & Gyn* 17 (4): 115, Dec. 1974.
4. *Fuchs, K., Brandes, J. M., Paldi, E.*: Enhancement of ovulation by chorion for successful artificial insemination. *Int J Fertil* 11: 211, 1966.
5. *Guttmacher, A. F.*: Role of artificial insemination in treatment of sterility. *Obstet Gynecol Surv* 15: 767, 1960.
6. *Kleegman, S. J., Kaufman, S. A.*: Infertility in women. Philadelphia, FA Davis, 1966, p. 165.
7. *Rosenberg, A. H.*: Legal aspects of artificial insemination. *N Engl J Med* 278: 552, 1968.
8. *Rubin, B.*: Psychological aspects of human artificial insemination. *Arch Gen Psychiatry* 13: 121, 1965.
9. *Thomas, H. H.*: Diagnosis in infertility. *Fertil Steril* 6: 779, 1966.
10. *Tyler, E. T.*: The clinical use of frozen semen banks. *Fertil Steril* 24: 413, 1973.
11. *Weinberger, A.*: Partial solution to legitimacy problems arising from the use of artificial insemination. *Indiana Law J* 35: 143, 1960.

1. *Behrman, S. J.*: Artificial Insemination, in Progress In-

*COMMENTARY:*  
**CONSERVATIVE TREATMENT OF SPLENIC  
INJURIES IN CHILDREN**

Pedro J. Rosselló, M. D.

The standard treatment for splenic laceration or rupture has been splenectomy. This well accepted surgical principle has been applied uniformly to include any injury of the spleen, no matter how trivial. The basis for this is the concept that the spleen has a poor healing capacity. This approach has been further reenforced by the technical ease and low complication rate of splenectomy.

Recently there has been an increasing awareness that splenectomy in children is not totally innocuous. The splenectomized pediatric patient is at high risk of developing overwhelming sepsis and death (2, 3, 4, 5, 6). On the other hand evidence is accumulating that demonstrates that the traumatized spleen is capable of healing itself (7, 8, 9, 10, 11).

At Children's Hospital Medical Center, Boston, we followed during the period from 1973-76, a group of children with documented splenic rupture. One group with injury confirmed by technetium scans, was treated by careful observation (including hourly vital signs, central venous pressure, and urine output measurements) and non-operative support (nasogastric suction, intravenous fluids and transfusions). Eight of ten patients had a significant drop in the hematocrit, four required transfusions from 25-50 percent of their blood volume. Under

careful hospital observation, their course was uncomplicated, most being discharged after a 7-10 day hospitalization. There were no complications in the follow-up period which ranged from 3 months to 3 years.

In a second group, all patients had splenic injury documented at laparotomy. One patient underwent a hemi-splenectomy for a grossly shattered upper pole of the spleen. A post operative spleen scan showed good function, and there have been no complications in the follow-up period of over one year. The other three children had oversewing of simple lacerations. One of these subsequently died of other causes, and at autopsy there was no evidence of bleeding. The other two have had no complications. Details of these cases is extensively presented elsewhere (1).

Let us review the basis for the principle of splenectomy in injury to the spleen. Historically, this has been based on the poor results obtained in early series of ruptured spleen, where mortality reached nearly 100 percent without surgical intervention (12, 13). This high mortality was impressively reduced with splenectomy. No adverse complications seemed to follow a well performed splenectomy.

Recently a large volume of evidence is accumulating suggesting that the spleen is important in the immunologic defenses of the child (20, 21, 22, 23, 25). Many series have shown a greater risk of developing overwhelming sepsis and a death following a splenectomy in childhood (2, 3, 4, 5, 6). This

risk increases in the younger patient and in those having other underlying systemic diseases. The period at risk is not limited to childhood but sometimes may extended well into adult life (14). Penicillin prophylaxis has been recommended for indefinite periods in children who have undergone splenectomy (29).

What is needed to protect against this predisposition to sepsis? Apparently, a fairly intact spleen with its normal vascular supply is required. Experiments in animals have demonstrated a decreased effectiveness of implanted pieces of spleen in protecting against a bacterial challenge (17), and a similar situation appears to occur in man (14). Susceptibility to severe infections also exists in cases of congenital asplenia and of functional asplenia of sickle cell disease (15, 16). The dual splenic functions of producing antibodies and of acting as a trap for blood-borne infections, seem to be necessary to protect against severe sepsis caused by encapsulated bacteria.

On the other hand, what dangers are involved in allowing a traumatized spleen to remain in situ?

Uncontrolled bleeding with potentially fatal hemorrhagic shock is the most obvious and immediate possibility. This would constitute a clear indication for surgical intervention, as for any other life-threatening hemorrhage. However, in the great majority of cases the bleeding is self-limited, and with close monitoring, cases of massive or uncontrolled hemorrhage can be safely identified and treated surgically. Delayed splenic rupture, another possible complication has been well documented. Although figures as high as 10-15 percent of splenectomies are reportedly done for delayed rupture, the true risk of this occurrence when properly defined, is closer to 0.3-2 percent in adults (18, 19). Children have a decreased incidence of this complication as compared to adults. Although cases of delayed rupture have been reported as late as six months after injury, the incidence of this occurrence

falls rapidly after 4 to 5 days. The possibility of late occurrence of splenic cyst is present. However, this risk is low and would involve splenectomy at a later date under elective conditions. The vast majority of children would not require splenectomies.

Is there evidence to support the ability of the spleen to heal traumatic injuries? Experimental work on dogs and monkeys has demonstrated the capacity of the spleen to scar and heal without delayed complications (8, 10). Furthermore, there is clinical evidence that this also applies to humans. Douglas and Sympton reported a series of children with clinically diagnosed ruptured spleen, treated conservatively with good results (7). Mis-halany has reported a series of ten consecutive cases of splenic rupture diagnosed at laparotomy (9). In eight of these, simple suturing of the spleen was performed without late complications. Serial spleen scans and arteriograms demonstrated progression of healing in one of these cases.

Based on all these factors we feel that a conservative approach should be followed in traumatic injury of the spleen in children. A stepwise management plan for these cases is shown in Figure 1. In blunt abdominal trauma (group 1) the initial approach should include diagnostic test, (including a scan or arteriogram), supportive therapy, and careful monitoring of vital signs, central venous pressure, and hematocrit changes.

This presupposes round the clock follow-up in an intensive care or quasi intensive care facility and rapid availability of operating room facilities at any time. If bleeding subsides then the non-operative approach should be continued. If greater than one third of the estimated blood volume needs to be transfused, then a laparotomy is indicted. Group II consists of cases with penetrating abdominal injuries, intraoperative splenic tears, or those with other intra-abdominal injury, that of itself, requires laparotomy. In these cases, an effort should be made to preserve normal splenic tissue. Lacera-



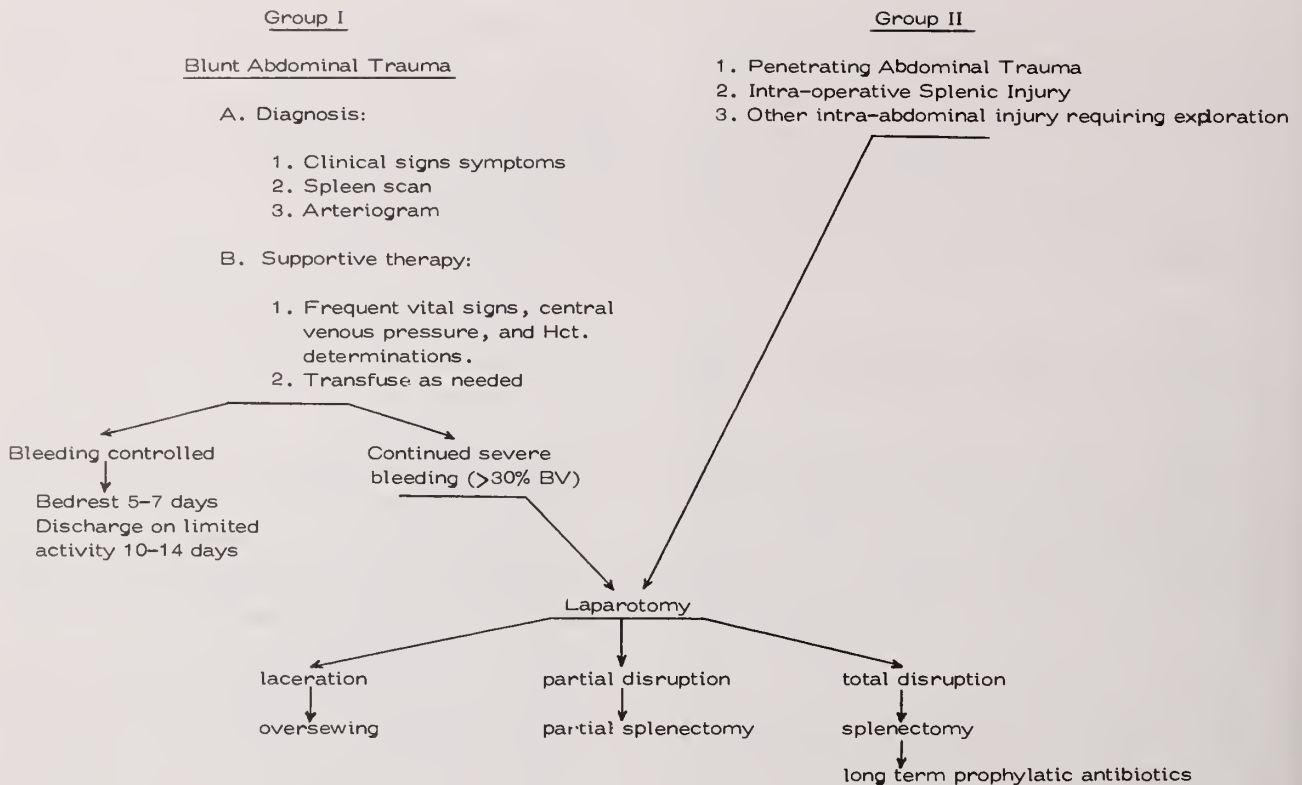


Figure 1: Management Plan for Splenic Injury in Children

tions should be oversewn. Partial disruption may require partial splenectomy. Only in cases where there is total disruption of the spleen, or if bleeding is not controlled, should a total splenectomy be carried out. The younger the patient, the greater the efforts to preserve normal splenic tissue should be. One must emphasize that this approach should be followed only if one can assure adequate monitoring of the child with hourly measurement of vital signs, central venous pressure and urine output. Otherwise the risk of an undetected potentially lethal hemorrhage outweighs the risk of splenectomy. Furthermore, this approach is recommended only for the pediatric patient, and should not be extended to the adult, since the incidence of post splenectomy infections does not appear to increase markedly in this latter group. One situation that might be applicable

to the adult is that of the iatrogenic tears occurring during other abdominal procedures. A higher incidence of complications is well documented when splenectomy is carried out in these cases (27), and these might be decreased by an adequate repair of the laceration.

## References

1. Rosselló, P., Eraklis, A. J.: Should the injured spleen be removed? Submitted for publication.
2. Eraklis, A. J., Kevy, S. V., Diamond, L. K.: Hazards of Overwhelming Infections After Splenectomy in Childhood. *NEJM* 276, 1225, 1967.
3. Eraklis, A. J., Filler, R. M.: Splenectomy in Childhood. *J. Pediat. Surg.* 7, 382, 1972.
4. Erikson, W. D., Burgert, E. O., Lynn, H. B.: The hazards of severe infection following splenectomy in children. *Am. J. Dis. Childhood* 116: 1, 1968.
5. Smith, C. H., Erlandson, M., Schulman, I.: Hazards of severe

- infection in splenectomized infants and Children. Am. J. Med. 22: 390, 1957.
6. Balfanz, J. R., Nesbit, M. E., Jarvis, C., Krivit, W.: Overwhelming Sepsis following splenectomy for trauma. J. Pediat. 88, 458, 1976.
7. Douglas, G. J., Simpson, J. S.: The conservative management of splenic trauma. J. Pediat. Surg. 6, 565, 1971.
8. Upadhyaya, P., Nayak, N. C., Moitra, S.: Experimental Study of splenic trauma in monkeys. J. Pediat. Surg. 6, 767, 1971.
9. Mishalany, H.: Repair of the ruptured spleen. J. Pediat. Surg. 9, 175, 1974.
10. De Boer, J., Summer-Smith, G., Downie, H. G.: Partial Splenectomy: technique and some hematologic consequences in Dog. J. Pediat. Surg. 7, 378, 1972.
11. Matsuyama, S., Suzuki, N., Nagamachi, Y.: Rupture of the spleen in the newborn: treatment without splenectomy. J. Pediat. Surg. 11, 115, 1976.
12. Bailey, H.: Traumatic rupture of normal spleen. Br. J. Surg. 15, 40, 1927.
13. Maze, W.: Traumatic Rupture of the Spleen. J. Pediat. 26, 82, 1945.
14. Hyslop, N. E., McCluskey, R.: Fever and Circulatory Collapse in an Asplenic Man. NEJM 293: 547, 1975.
15. Bismo, A. L., Freeman, J. C.: The syndrome of asplenia, pneumococcal sepsis and disseminated intravascular coagulation. Ann. Int. Med. 72: 389, 1970.
16. Kevy, S. V., Tefft, M., Vawter, G., Rosen, F.: Hereditary splenic hypoplasia, Pediatrics 42: 752, 1968.
17. Crosby, W. H., Benjamín, N. R.: Frozen spleen keimplanted and challenged with Bartonella. Am. J. Pathol. 39, 119, 1961.
18. Benjamín, C. I., Engrav, L. H., Perry, J. F.: Delayed rupture or delayed diagnosis of rupture of the spleen. S. G. O. 142, 171, 1976.
19. Lorimer, W. J.: Occult rupture of the spleen. Arch. Surg. 89: 434, 1964.
20. King, H., Shumacker, H. B.: Splenic Studies: Susceptibility to infection after splenectomy performed in infancy. Ann. Surg. 136: 239, 1952.
21. Haller, J. A.: Role of the spleen in experimental neonatal infections and transplanatation. J. Pediat. Surg. 5, 1972, 1970.
22. Constantopoules, A., Najjar, V. A., Smith, J. W.: Tuffsin deficiency: A new syndrome with defective phagocytosis. J. Pediat. 80: 564, 1972.
23. Najjar, V. A., Nishioka, K.: Tuffsin a physiological phagocytosis stimulating peptide. Nahire, 228, 672, 1970.
24. Rowly, J.: Formation of circulatory antibodies in splenectomized antibodies in splenectomized animals. J. Immunol. 65: 515, 1950.
25. Whitaker, A. N.: Effect of previous splenectomy on the course of pneumococcal bacteremia in mice. 95, 357, 1968.
26. Shinefield, H., Steinberg, C., Kaye, D.: Effect of splenectomy on the susceptibility of mice inoculated with Diplococcus pneumonia. J. Exp. Med. 123: 777, 1966.
27. Croffiro, W., Schein, C. J., Gliedman, M. L.: Splenic injury during abdominal surgery. Arch. Surg. 111, 167, 1976.
28. Roy, M., Geller, J. S.: Increased morbidity of iatrogenic splenectomy. SGO 139: 392, 1974.
29. Shurin, S. B.: Prevention of severe infections following splenectomy: Policy statement of division of hematology and oncology, Children's Hospital Medical Center, Boston, March, 1976.

## LAS PRUEBAS CUTANEAS Y LA ALERGIA A PENICILINA

Carlos F. León Valiente, MD y Carlos H. Ramírez Ronda, MD, FACP

**Abstract:** Penicillin is an antibiotic frequently used; unfortunately, a small number of patients have allergic reactions. These reactions are of these three types: anaphilactic, serum sickness or dermatitides. The skin tests to determine penicillin hypersensitivity are presented and the immunologic mechanism discussed. The use of the benzylpenicillin skin test is contraindicated. The penicilloil polylysine (PPL) skin test, when negative, does not exclude all the patients that can have an anaphilactic reaction, but these patients can be excluded with a minor determinant mixture skin test. Unfortunately, this last test is not commercially available. The skin tests to determine penicillin allergy have a limited use at present and when used, you must be aware of their limitations.

**Resumen:** La penicilina es un antibiótico usado frecuentemente. Desafortunadamente, un número pequeño de pacientes tiene reacciones alérgicas que pueden ser de tres tipos: anafiláticas, enfermedad del suero y dermatitides. Las pruebas de piel para determinar

sensitividad a penicilina se discuten con su mecanismo inmunológico. El uso de la prueba cutánea de benzylpenicilina está contraindicado. La prueba cutánea con polyilisina de peniciloil, cuando es negativa, no excluye por completo a los pacientes que tendrán una reacción anafiláctica, más estos se pueden excluir con una prueba cutánea con la mezcla determinante menor. Desafortunadamente, esta segunda prueba no se consigue comercialmente. Las pruebas cutáneas para determinar alergia a penicilina tienen un uso muy limitado, y debe de conocerse sus limitaciones.

La penicilina fue aislada por Fleming en 1929 del microorganismo *Penicillium notatum* y fue introducida en 1941 a uso médico por Florey y Chain. Su núcleo básico, común a todas las penicilinas es el ácido 6-aminopenicilínico, un dipéptido cíclico formado por L-cisteína y D-valina. Cambiando las diferentes radicales añadidas a este núcleo básico se obtienen las diferentes formas de penicilina.

Las penicilinas son los antibióticos más usados (1). Es uno de los antibióticos más efectivos y permanece como el antibiótico de elección para la mayoría de las infecciones por bacterias sensibles. Entre estas tenemos: infección por *Streptococcus pyogenes*, como faringitis, celulitis, fiebre escarlatina y septicemia; *Streptococcus pneumoniae* (neumococo), en infecciones pulmonares del adulto, en otitis media estreptocócica, meningitis bacteriana, tétano, difteria, gonorrea, sífilis y muchas otras

---

De la Sección de Enfermedades Infecciosas, Departamentos de Investigación y Medicina, Hospital de Veteranos y la Escuela de Medicina de la Universidad de Puerto Rico, San Juan, Puerto Rico.

Favor de pedir reproducciones a: Carlos H. Ramírez-Ronda, MD, Jefe, Laboratorio de Investigación de Enfermedades Infecciosas (151), Hospital de la Administración de Veteranos, GPO Box 4867, San Juan, Puerto Rico 00936.



infecciones bacterianas; así como en la profilaxis mensual de fiebre reumática.

Desafortunadamente, a pesar de su efectividad, encontramos efectos tóxicos, aunque pocos (2). Entre estos tenemos reacciones de hipersensibilidad. Las reacciones de hipersensibilidad pueden ser de 3 tipos: reacción inmediata o anafiláctica, enfermedad del suero y dermatitis por contacto.

### Reacciones de Hipersensibilidad a Penicilina

#### *Reacción Inmediata o Anafiláctica*

La reacción anafiláctica es rara y ocurre en pacientes ya sensibilizados (3). Su incidencia es de 0.004 a 0.04 por ciento de pacientes tratados con penicilina. La mortalidad asociada es de alrededor de 10 por ciento. Clínicamente se manifiesta por náusea, palidez, taquicardia, broncoespasmos y "shock". Su tratamiento está basado en el uso de adrenalina. Se pueden utilizar torniquetes, medidas contra el "shock" y esteroides.

#### *Enfermedad del Suero*

Esta manifestación de hipersensibilidad es más frecuente que la reacción anafiláctica, aunque menos temida. Tiene una incidencia de 1 a 7 por ciento. Usualmente ocurre entre 7 a 10 días después de la primera administración de penicilina y clínicamente se manifiesta con fiebre, malestar general, urticaria, dolores articulares y en ocasiones edema angioneurótico. El cuadro puede presentarse como una dermatitis exfoliativa o como el síndrome de Stevens-Johnson. Es importante anotar que la velocidad de sedimentación está normal (2).

#### *Dermatitis por Contacto*

Es una manifestación frecuente y resulta de la aplicación local de productos que contienen penicilina. Se ve con frecuencia en personal paramédico, como enfermeras y la forma más

efectiva de tratamiento es evitar la reacción, no utilizando productos dérmicos que contengan penicilina o sus derivados (2).

#### *Reacciones Locales*

Las reacciones locales no son reacciones de hipersensibilidad pero pueden interpretarse como "alergia" y se manifiestan por enrojecimiento e hinchazón en área de la inyección. La interpretación errónea resulta en marcar pacientes como "alérgicos" a penicilina cuando en realidad no lo son.

### Mecanismo de Hipersensibilidad

El mecanismo básico de estas reacciones es complejo y como resultado varios investigadores han postulado varias teorías. Las reacciones de hipersensibilidad y la sensitización a la penicilina usualmente resultan por sensitización después del uso previo de la misma. Algunos pacientes desarrollan una reacción al tener contacto con penicilina como medicamento por primera vez. En estos casos se sospecha que el paciente ha estado en contacto con penicilina o el núcleo de penicilina en alguna forma; por ejemplo, con el consumo de leche contaminada con penicilina.

Los compuestos responsables de las reacciones de hipersensibilidad han sido investigados ampliamente. Inicialmente se alegó que se debía a la presencia de impurezas en los preparados comerciales, incluyendo proteínas de alto peso molecular. Este concepto se descartó después de determinar que el núcleo básico de la molécula de penicilina de por sí, podía provocar sensitización. Se postuló entonces que dicho núcleo actuaba como un hapteno, combinándose con proteínas séricas para formar un compuesto antigénico.

Conocemos que la molécula de penicilina en sí no se combina frecuentemente con proteínas para producir un compuesto antigénico y que los haptenos se forman con sus productos

metabólicos. El más importante de los productos metabólicos es el compuesto peniciloil, derivado directamente del núcleo de penicilina o a través de un compuesto intermedio, el ácido 6-amino-penicilínico. Es peniciloil el compuesto que se combina con las proteínas séricas y forma un conglomerado llamado el "determinante antigénico mayor" (DAM). Además de peniciloil hay otros productos de degradación como el ácido peniciloico, el ácido peniloico y otros que también se han relacionado con sensitización y se conocen como "determinantes antigénicos menores". Estos determinantes menores son responsables por la reacción de anafilaxis (4). Todas las penicilinas tienen un núcleo común y el ácido 6-aminopenicilínico y otros derivados están presentes en todas las penicilinas, por lo tanto se infiere que una vez un paciente está sensitizado a una penicilina, está sensitizado a todas (6). El DAM por sí solo no puede usarse en pruebas cutáneas ya que es un potente componente antigénico, pero cuando se combina en un polímero de lisina, se forma la polyilisina de peniciloil (PPL); puede usarse como prueba cutánea más determinada la sensibilidad al DAM solamente (5).

### Determinación de Hipersensibilidad

#### *Evaluación Clínica*

El clínico tiene necesariamente que basarse en un buen historial médico para determinar qué personas podrían ser alérgicas a la penicilina. Pacientes con historial de asma bronquial, fiebre de heno y otras reacciones alérgicas están predispuestos a desarrollar alergia a la penicilina.

### Pruebas Cutáneas

#### *Prueba con benzylpenicilina*

Las pruebas cutáneas que se usan de rutina, usando el compuesto benzylpenicilina como antígeno, no son aconsejables porque aún usando pequeñas dosis pueden causar reacciones severas y sensibilizar a la persona o

causar anafilaxis.

#### *Prueba con polyilisina de peniciloil*

La prueba de piel utilizando el compuesto de polyilisina de peniciloil es considerada más segura, aunque se han reportado casos de reacciones alérgicas (5). Esta prueba tampoco detecta todos los candidatos potenciales a tener reacciones inmediatas o de anafilaxis.

### Mezcla de Determinantes Mayores y Menores

El valor predictivo de las pruebas cutáneas aumenta si en adición a la prueba de polyilisina de peniciloil se usa una prueba utilizando una mezcla de los determinantes menores (7). De esta manera, usando ambas pruebas, se puede predecir y excluir al paciente que tendrá una reacción inmediata, ya que si ambas pruebas son negativas, la incidencia de alergia es baja, ya sea de reacciones inmediatas o tardías. El problema mayor es que esta prueba no está disponible de fuentes comerciales y solo se está usando en protocolos experimentales.

### Manejo del Paciente

Nuestras recomendaciones sobre el manejo del paciente que va a recibir penicilina es como sigue: Lo más importante es obtener un historial sobre reacciones previas a penicilina, de tener un historial positivo y una condición benigna, debe utilizarse un antibiótico alternativo, erytromicina, las cefalosporinas o clindamicina. Si el paciente tiene una condición seria de vida o muerte, donde el uso de penicilina puede salvar la vida, el paciente puede desensitizarse en un área de cuidado intensivo listos para tratar anafilaxis, de ocurrir ésta (8). Si el historial de reacciones previas es negativo, usualmente puede usarse la penicilina, tomando la precaución de observar al paciente por 30 minutos. La prueba de piel con benzylpenicilina está contraindicada. Si

usted tiene la facilidad para hacer pruebas de piel con polyisina de peniciloil, la prueba es efectiva pero aún siendo negativa no excluye a todos los pacientes que puedan tener anafilaxis, más una prueba positiva indica que el paciente no debe recibir penicilina bajo condiciones normales (9).

Para el médico poder prescribir penicilina a un paciente y estar seguro que no tendrá reacción anafiláctica, se requiere el uso de pruebas cutáneas con polyisina de peniciloil más la prueba con determinantes menores. El valor mayor del uso de las pruebas combinadas está en el manejo del paciente que tiene un historial de "alergia" a penicilina el cual por su descripción no es claro, en este paciente las pruebas cutáneas combinadas, de ser negativas, hacen factible el uso de la penicilina cuando indicado (10).

### Conclusiones

Las pruebas cutáneas para determinar la hipersensibilidad a penicilina no deben de hacerse rutinariamente. La prueba cutánea con benzylpenicilina está contraindicada. La prueba de polyisina de peniciloil, la cual se puede conseguir comercialmente, puede utilizarse, más debe de conocerse sus limitaciones. Si positiva, la penicilina no debe utilizarse; si negativa, no excluye las reacciones de hipersensibilidad primaria o anafilaxis. La prueba combinada es efectiva pero no se consigue comercialmente. El paciente que tiene un historial claro de hipersensibilidad no debe re-

cibir penicilina. Las pruebas de piel pueden utilizarse para determinar hipersensibilidad a productos mayores en el paciente con un historial alérgico incierto reconociendo, que de ser negativas, no excluimos al paciente con anafilaxis. Siempre que se utilice penicilina en un paciente debemos observarlo por 30 minutos y tener epinefrina 1:1000 a la mano.

### Referencias

1. Ramírez-Ronda, C. H., León-Valiente, C. and Bermúdez, R. H.: Las Penicilinas. Bull P R Med Assoc 69: 134, 1977.
2. Annotation: "Hypersensitivity to penicillin". Lancet 1: 1204, 1967.
3. American Academy of Pediatrics Committee on Drugs: Anaphylaxis. Pediatrics 51: 136, 1973.
4. Levine, B. B., Redmond, A. P., Fellner, M. J. et al: Penicillin allergy and the heterogenous immune response of man to benzyl penicillin. J Clin Invest 45: 1895-1906, 1966.
5. Budd, M. A., Parker, C. W., Norden, C. W.: Evaluation of intradermal skin tests in penicillin hypersensitivity. JAMA 190: 203-205, 1964.
6. Batchelor, F. R., Dedwney, J., Feinberg, J. G. and Weston, R. D.: A 6-Aminopenicillanic acid. Lancet 1: 1175, 1967.
7. Voss, H. E., Redmond, A. P. and Levine, B. B.: Clinical detection of the potential allergic reaction to penicillin by immunologic tests. JAMA 196: 679-683, 1966.
8. Green, G. R.: Antibiotic therapy in patients with a history of penicillin allergy. In: Penicillin Allergy, eds., Stewart, G. T., McGovern, J. P., Springfield, Illinois, Charles C. Thomas, 1970, pp. 162-175.
9. "Testing penicillin allergy". J Indian Med Assoc - Editorial 61: 194-6, 1973.
10. Adkinson, N. F., Jr., Thompson, W. L., Maddrey, W. C. and Lichteinstein, L. M.: Routine use of penicillin skin testing on an inpatient service. New Engl J Med 285: 22, 1971.



## NUEVOS CONCEPTOS EN LA PATOFISIOLOGIA DE HIPERTENSION

José L. Cangiano, MD

En la actualidad, la hipertensión arterial es posiblemente, la enfermedad de mayor prevalencia en el mundo. Estudios epidemiológicos han establecido el desenlace catastrófico de una hipertensión no controlada. La enfermedad puede atacar devastadoramente el cerebro, corazón, riñones y vasos periféricos. La causa de hipertensión es desconocida en el 90 por ciento de los casos. Solamente en el 10 por ciento puede identificarse la causa, la cual se origina de una enfermedad endocrinológica o renal.

Estudios estadísticos en los Estados Unidos de América han demostrado que la hipertensión prevalece en 10 por ciento de la población, lo cual abarca de 20 a 22 millones de personas. Encontramos hipertensión primaria o de origen desconocido en alrededor de 18 a 20 millones de personas e hipertensión secundaria (endocrina o renal) en 2 a 4 millones de personas. En otros países, incluyendo los países latinos, no se pueden aplicar estas estadísticas, ya que hay una amplia variación de diferencias étnicas, genéticas, dietéticas y del medio ambiente. Por ejemplo existe una raza indígena en la frontera de Brazil y Venezuela donde la incidencia de hipertensión es sumamente baja lo cual se ha correlacionado a las cantidades ínfimas de sal que consumen en su dieta estos indígenas.

Por el contrario, en Honshu, isla del archipiélago japonés, se ha documentado una alta incidencia de hipertensión con complicaciones cardiovasculares y alta mortalidad correlacionándose a una alta ingesta de sal en la dieta.

A pesar de los grandes avances en el entendimiento de los mecanismos envueltos en hipertensión primaria, se desconoce la secuencia precisa de estos mecanismos en su fisiopatogenia. Se creyó por un tiempo que el sistema renina-angiotensina-aldosterona explicaría de una forma unificada el problema de la hipertensión. Sin embargo, el problema aparece ser uno más complicado envolviendo diferentes sistemas y mecanismos fisiológicos interrelacionados, lo cual ha dado origen a la visión pluralística de hipertensión.

La investigación de cepas de ratas espontáneamente hipertensas nos ha permitido una visión más amplia y definida de la fisiopatología envuelta en hipertensión. Estas ratas, al igual que los humanos, no nacen hipertensas pero al cabo de varios meses y después de llegar a 200 a 300 mg de peso se nota una elevación de la tensión arterial. Las cepas que se han desarrollado son las Okamoto, Dahl, Milán y Nueva Zelandia. Se ha establecido que hay una disfunción renal primaria, ya sea por influencia extrínseca o intrínseca en el riñón. El sistema simpático (influencia extrínseca) aparenta estar envuelto en ratas Okamoto y Nueva Zelandia mientras que en las cepas de Milán y Dahl aparenta estar envuelto el riñón de forma intrínseca. La influencia extrínseca en ratas Okamoto y Nueva

TABLA I  
PATRONES HEMODINAMICOS EN HIPERTENSION

	Débito Cardíaco	Resistencia Periférica
<i>Hipertensión Lábil</i>	↑	N    o    ↓
<i>Hipertensión Renal Vascular</i>	↑	N    o    ↑
<i>Hipertensión Esencial</i>	N	↑
<i>Aldosteronismo Primario</i>	N	↑
<i>Hipertensión Renal Parenquimatosa</i>		
<i>a) Glomerulonefritis aguda</i>	↑	N
<i>b) Crónico no azotémico</i>	N	↑
<i>c) Urémico</i>	↑	↑

TABLA II  
VOLEMIA EN HIPERTENSION

<i>Aumentada</i>	<i>Hipertensión esencial 30-40 por ciento</i> <i>Aldosteronismo Primario</i> <i>Enfermedad renal etapa final 80-90 por ciento</i> <i>Glomerulonefritis aguda</i>
<i>Disminuída</i>	<i>Hipertensión esencial</i> <i>Feocromocitoma</i> <i>Estenosis de la arteria renal</i>

Zelandia es evidenciado por:

1. Un aumento en la descarga simpática beta
2. Disminución de la tensión arterial por inmunosimpatectomía.
3. Aumento de la reactividad cardiovascular por estímulos irritativos.
4. Deceleración en el desarrollo de hipertensión al mantener la rata en ambiente oscuro y plácido.

5. Falta de provocar hipertensión al transplantar un riñón de estas ratas a otra.

Asimismo la influencia intrínseca renal en las ratas Dahl y Milán se pone de manifiesto cuando:

1. Se provoca la hipertensión al transplantar el riñón.
2. Se demuestra una sensitización en la ingestión de sodio.

TABLA III  
RENINA EN HIPERTENSION

<i>Aumentada</i>	<i>Hipertensión esencial</i> <i>Renovascular</i> <i>Renal parenquimatosa unilateral</i> <i>Hipertensión maligna</i> <i>Enfermedad renal de etapa final -10-20 por ciento</i>
<i>Normal</i>	<i>Hipertensión esencial</i>
<i>Disminuída</i>	<i>Aldosteronismo primario</i> <i>Aldosteronismo pseudo primario</i> <i>Exceso de 18 desoxy-corticosterona</i> <i>Deficiencia de hidroxilasa 11 y 17</i> <i>Síndrome de Cushing</i> <i>Hipertensión esencial</i>

TABLA IV  
SISTEMA NEUROVEGETATIVO EN HIPERTENSION

<i>Aumentado</i>	<i>Hipertensión esencial</i> <i>Estenosis arterial renal</i> <i>Feocromocitoma</i> <i>Hipertensión lábil</i>
------------------	---

3. En la cepa Milán se encuentra una retención de sodio y agua al disminuir la filtración glomerular y la fracción de filtración.

En el humano, como en la rata, podrían estar envueltos diferentes mecanismos que manifiesten la tensión arterial elevada lo cual podría explicar por qué algunas formas de terapia son más beneficiosas para algunos pacientes que otros.

El amplio espectro de anormalidades fisiológicas produciendo hipertensión envuelve una

interrelación cuantitativa de factores que incluyen el débito cardíaco, la resistencia periférica, el volumen intravascular, el sistema renina angiotensina y el sistema neurovegetativo. Se ha podido clasificar la hipertensión de acuerdo a la anomalía fisiológica presente. Las tablas del I al IV presentan el patrón de anormalidad correlacionado al tipo de hipertensión. Esta relación tiene importancia tanto diagnóstica como terapéutica.

El control diario de la presión es el resultado de la puesta en juego de reflejos cardiovasculares originándose en los baroreceptores



carotídeos y quimorreceptores. El estímulo de los baroreceptores carotídeos evita una descarga simpática de origen central, lo cual resulta en una disminución del débito cardíaco, bradicardia y finalmente disminución de la tensión arterial. El sistema neurovegetativo responsable de estos resultados ha recibido una mayor atención de los investigadores, ya que muy bien la hipertensión primaria puede ser de origen central neurológico.

La hipertensión de origen renal se puede dividir en vascular y parenquimatosa. La hipertensión debido a estenosis de la arteria renal depende mayormente del sistema renina-angiotensina-aldosterona. Una hipoperfusión del riñón estimula la descarga de renina del aparato yuxtaglomerular, la cual actúa sobre la globulina alfa 2 y desencadena la formación de angiotensina I y II. Angiotensina II es el vasopresor más potente que existe en el cuerpo y además tiene la peculiar característica de estimular la zona glomerulosa de la glándula adrenal haciéndola segregar aldosterona. Esto a su vez estimula la reabsorción de sodio y agua en el tubulo distal del nefrón. Desde el punto de vista teleológico, este mecanismo está envuelto en la conservación de agua y sal para mantener la homeostasis del cuerpo. Un proceso patológico que mantenga una hipertensión total o parcial renal, perpetúa la producción de renina y la formación de angiotensina II. El mejor criterio diagnóstico para la cura quirúrgica de este morbo es la determinación de la renina diferencial de las venas renales. Cuando la razón de la concentración de renina del lado afectado al no afectado rebasa 1.5, estimamos existe una relación de causa y efecto entre la lesión y la hipertensión. Esta prueba ha demostrado ser confiable en más del 90 por ciento de los casos examinados.

De la hipertensión de origen parenquimatosa renal se ha postulado que los siguientes mecanismos son importantes en la genesis.

1. el eje renina-angiotensina-aldosterona
2. ingesta excesiva de sal y agua.

3. la ausencia de vasodepresores como prostaglandinas o sistema Kallikreina.
4. una combinación de los factores arriba mencionados.
5. la presencia de sustancias vasopresoras aún desconocidas.

En la actualidad, la hipertensión que acompaña la glomerulonefritis aguda y alrededor de 90 por ciento de los casos de uremia se asocian a exceso de sal y agua. La restricción de sal en la dieta y la remoción de sal por diálisis pueden mejorar y hasta curar esta forma de hipertensión. En alrededor de 10 por ciento de los casos de hipertensión urémica se ha implicado el sistema renina-angiotensina. En estos casos la remoción de sal y agua no altera el curso de la hipertensión y la renina del plasma consistentemente permanece elevada. La nefrectomía bilateral disminuye pronta y sostenidamente la tensión arterial. Antes de considerar cirugía se debe hacer un intento en disminuir la tensión arterial con medicamentos potentes como nitroprusiato, minoxidil o ganglioplégicos. De no ser posible controlar la presión entonces se debe considerar la nefrectomía bilateral, ya que el riesgo de una hipertensión descontrolada es catastrófico. Es de gran importancia considerar que estos riñones, aunque no funcionan desde el punto de vista de excreción de productos metabólicos, son órganos endocrinos y están envueltos en la producción de metabolitos de Vitamina D para absorber calcio del intestino y en la genesis de eritropoietina para la formación de glóbulos rojos. Al remover los riñones los requerimientos de calcio y transfusiones de sangre pueden aumentar en estos pacientes.

En la hipertensión asociada a azotemia (elevación de la urea sanguínea sin síntomas) se desconocen los mecanismos precisos y como consecuencia la terapia no es específica. El uso de agentes hipotensores en estos casos está indicado.

Las siguientes enfermedades pueden estar asociadas a la hipertensión de origen endocrino:

1. hipertiroidismo o hipotiroidismo
2. hiperparatiroidismo
3. acromegalia
4. hiperadrenalismo

El hiperadrenalismo ha sido la más estudiada y se ha encontrado que el problema puede residir en la corteza o en la médula. En la corteza con 1) tumores usualmente benignos produciendo aldosteronismo primario o 2) hiperplasia o tumores malignos produciendo aldosteronismo pseudoprimario y síndrome de Cushing. En la médula cobra importancia la secreción excesiva de catecolaminas o sus metabolitos, lo cual puede ser debido a un tumor benigno o maligno como un feocromocitoma.

En aldosteronismo primario hay una producción excesiva de aldosterona. Aunque el mecanismo por el cual se produce hipertensión es completamente desconocido, se encuentra que la renina está disminuída y suprimida a estímulos fisiológicos tales como dieta baja en sal y al asumir la posición erecta. La volemia y la resistencia vascular periférica están aumentadas. También se encuentran una hipernatremia relativa y una disminución del potasio sanguíneo, producto de una excesiva excreción de potasio.

De un 10 a 20 por ciento de los pacientes con hipertensión primaria tienen supresión de la renina sin aldosterona elevada. En algunos de estos pacientes se han encontrado elevados otros mineralocorticoides tales como 18 hidroxycorticosterona, DOC y 16  $\beta$ -hidroxidehidroepiandrosterona. Sin embargo en la gran mayoría de los hipertensos hiporeninémicos no se ha encontrado elevación de estos mineralocorticoides.

En los casos de aldosteronismo primario por adenoma adrenal, la cirugía está indicada y cura la gran mayoría de los casos. Sin embargo, la cirugía no cura la hipertensión que se asocia a hiperplasia (aldosteronismo pseudoprima-

rio). El uso de espironolactona (aldactona) ha ganado mucho interés en el tratamiento de esta hipertensión. Estudios extensos por varios investigadores y nuestros laboratorios han demostrado que espironolactona tiene un efecto diurético primario al bajar inicialmente la tensión arterial.

Podemos asegurar que a medida que pasa el tiempo estaremos más convencidos que la hipertensión no se produce en una forma simple con un solo mecanismo definido. Creemos que el estado hipertenso resulta de una alteración de varios factores fisiológicos interrelacionados, los cuales pueden variar en diferentes etapas de su desarrollo. Esto explicaría la aparente disociación de mecanismos con el nivel de tensión arterial que actualmente se encuentra en hipertensión experimental. Por ejemplo, nuestros estudios preliminares han documentado la disociación de renina y el nivel de tensión sistólica en ratas hipertensas después de ligar la arteria renal izquierda. Al comienzo de la hipertensión, la renina se mantiene normal y es al cabo de 7 días después de la ligación que la renina empieza a aumentar para luego bajar a normal en tres semanas. Que factor escala inicialmente la tensión arterial y que factor sostiene más tarde esa hipertensión son un enigma que está bajo investigación al presente. Los mecanismos neurogénicos probablemente cobrarán mayor importancia y dedicación en la investigación futura en las causas de hipertensión.

Esperamos que en la próxima década se produzcan grandes avances que permitan el esclarecimiento de la fisiopatología de la hipertensión lo cual significaría una terapia más racional, juiciosa y efectiva. Mientras esperamos estos nuevos descubrimientos no nos debemos olvidar de seguir controlando al hipertenso con las drogas antihipertensivas disponibles y de recomendar a todo paciente la eliminación de los factores de riesgo como el cigarrillo, sobrepeso, exceso de sal y sobre todo las tensiones emocionales.



# TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE **DYAZIDE®**

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### Warning

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**Indications:** When the combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium sparing action of triamterene is warranted. (See Box Warning.) Routine use of diuretics in healthy pregnant women is inappropriate; they are indicated in pregnancy only when edema is due to pathological causes.

**Contraindications:** Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K<sup>+</sup> levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K<sup>+</sup> intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids).

Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K<sup>+</sup> frequently; both can cause K<sup>+</sup> retention and elevated serum K<sup>+</sup>. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis.

'Dyazide' interferes with fluorescent measurement of quinidine.

### Adverse Reactions:

Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions;

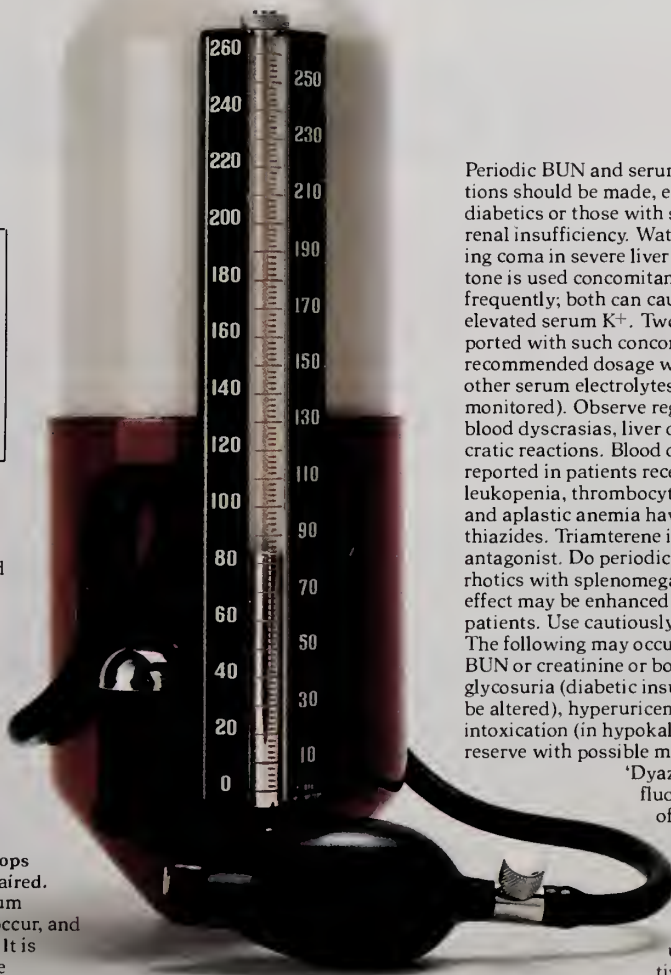
nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

**FOR LONG-TERM CONTROL  
OF HYPERTENSION\*  
SERUM K<sup>+</sup> AND BUN SHOULD  
BE CHECKED PERIODICALLY.  
(SEE WARNINGS SECTION.)**

SK&F CO., Carolina, P.R. 00630

**SK&F CO.**  
a SmithKline company







**Only 1  
tablet B.I.D.**

**New convenience**  
**Gantanol<sup>®</sup> DS**  
sulfamethoxazole/Roche  
double-strength dosage form  
for acute cystitis\* patients

\*nonobstructed; due to susceptible organisms

New Gantanol® DS (sulfamethoxazole) tablets offer even greater convenience and economy for your patients with acute, nonobstructed cystitis due to susceptible strains of *E. coli*, *Klebsiella-Aerobacter*, staphylococcus, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*...

The same amount of medication, the same efficacy, with only *half* the number of tablets per day.

Simplified dosage regimen encourages patient compliance: 2 tablets (1 Gm each)

STAT—then 1 tablet B.I.D. for 10 to 14 days.

Clinical efficacy so basic you can start cystitis therapy even before culture results are available.

# and economy

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Acute, recurrent or chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, staphylococcus, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*), in the absence of obstructive uropathy or foreign bodies. Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

**Warnings:** Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under 12 with chronic renal disease.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness,

• In a clinical study of 406 patients on Gantanol (sulfamethoxazole) B.I.D., close to 9 out of 10 patients achieved negative urine cultures. While Gantanol tablets were used in this study, one Gantanol DS tablet has been proved bioequivalent to two Gantanol tablets.\*

Gantanol is contraindicated during pregnancy, during the nursing period, and in infants under 2 months. During therapy, maintain adequate fluid intake, perform frequent CBC's and urinalyses with careful microscopic examination.

\*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

**Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age** (except adjunctively with pyrimethamine in congenital toxoplasmosis). *Usual adult dosage:* 2 Gm (2 DS tabs or 4 tabs or 4 teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

*Usual child's dosage:* 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially; then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

**Supplied:** DS (double strength) tablets, 1 Gm sulfamethoxazole; Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

**Basic therapy with convenience and economy:**

**Gantanol®** (sulfamethoxazole)Roche®

**Basic therapy with even more convenience and economy:**

**Gantanol® DS** (sulfamethoxazole)Roche®



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



**BURROUGHS WELLCOME CO. MAKES  
CODEINE COMBINATION PRODUCTS.  
YOU MAKE THE CHOICE.**



**EMPIRIN<sup>®</sup>  
COMPOUND  
c̄ CODEINE  
#3**

Each tablet contains:  
codeine phosphate, 32 mg (gr ½),  
(Warning: May be habit-forming);  
aspirin, 227 mg; phenacetin, 162 mg;  
and caffeine, 32 mg.



**EMPRACET<sup>™</sup>  
c̄ CODEINE  
#3**

Each tablet contains:  
codeine phosphate, 30 mg (gr ½),  
(Warning: May be habit-forming);  
and acetaminophen 300 mg.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



## AMA NEWS:

*WHAT'S UP? MEDICAL BILLS ETC., ETC., ETC., ETC., ETC. . . .*

CHICAGO — What's up? Well, medical care prices are up-- that's for sure. Medical care was at 184.7 on the Consumer Price Index in 1976. (1967=100) Some people even say that medical care is the fastest rising item in the CPI.

But that's not true, says the American Medical Association. Many important items on the CPI (and some relatively trivial ones, too) are rising as fast as medical care -- or even faster.

That includes many essential services. Lawyers' charges, for example, were at 199.9 on the 1976 CPI. Insurance and finance charges were at 196.6. Postal charges were at 222.3.

Most services pertaining to everyday living are up: having your living room or dining room repainted (225.6), having the house roof resingled (233.4), having a sink replaced (210.2), having the furnace repaired (207.1), having the washing machine repaired (200.4), repairs of the family auto (189.7), services of a baby sitter for the evening (214.6).

Speaking of baby sitters and babies, the price of diapers registered 190.2 on the CPI while blue jeans were slightly behind at 190.0.

Coffee breaks and other between-meal snacks have also made impressive price rises: coffee was at 243.6, sugar at 201.3, evaporated milk at 204.8. Cinnamon rolls were at 195.9.

For the youngsters' snacks, the price of a cola drink was at 194.2, chocolate bars were at 233.5, cookies were at 189.6. The price of taking the kids to the movies, incidentally, hit 193.8 on the CPI.

The dinner table was affected by higher prices: Potatoes (200.1), rib roast (188.4), whole ham (199.6), seafood (227.3). Bacon for breakfast was at 210.4, sausage at 226.6. American cheese, popular in lunch boxes and picnics, was at 198.6.

Prices of many of the amenities of life have risen: toilet soap (193.5), women's haircuts (186.6), china dinnerware (190.6).

Bathroom tissue was at 234.4.

Of course, prices aren't the only things that have gone up. Incomes have risen, too. Per capita income after taxes has more than doubled since 1967, for an index of 202.0 in 1976.

And Social Security taxes have risen faster than either consumer prices or incomes. An index for the maximum Social Security tax on employees (if the government published one) would have been 308.2 in 1976 (1967=100). For 1977 the maximum Social Security tax index would be 332.4.

## COMPUTERS IN MEDICINE

The primary objective of medicine, today, is to improve the prevention and treatment of diseases by:

1. Increasing the level of diagnostic and therapeutic skills;
2. Making them accessible to those who require them; and
3. At a cost which is within the financial reach of the patient.

There is a growing body of opinion that the future of health care, specifically the achievement of these three objectives, is closely intertwined with the development of computer applications for the medical community.

The health care professional is faced not only with achieving objectives such as those, but with satisfying the many requirements imposed by operational necessity, external pressures and government regulations. Many professionals are reaching the point of overload in trying to maintain and improve patient care while complying with increased administrative demands and producing an adequate return. Compu-

ters have potential applications in some or all of the following:

- Improving patient care
- Creation, storage, maintenance and retrieval of medical records
- Improving diagnostic and therapeutic skills
- Reducing the rate of increasing costs
- Improving facility and personnel utilization
- Improving collection of accounts receivable
- Improving reporting to and payment from third parties
- Improving financial management and control

#### THE CONSULTATIVE SERVICES PROGRAM

The American Medical Association recognizes the potential computers have in the health care setting. It also recognizes that the professionals often do not have the time or technical training to efficiently or accurately answer the important questions:

- When are computer based services justified?
- What kinds of services are suitable now and what impact will growth and technological advances have?
- How are those services most efficiently implemented?

Because the use of computer based services represent a significant procedural and financial commitment in any health care setting, and because objective expertise on the use of computers in medicine has been scattered and not generally available, especially to the physician community, the American Medical Association initiated the Computer Systems in Medicine Consultative Services Program.

For the health care professional who is considering some form of computer service, as well as for current users, who want to improve or expand their computer applications, the AMA Consultative Services Program

can provide an objective viewpoint, expertise in both methods and equipment, and the time to evaluate what is feasible and what is desirable for the professional's needs.

#### SCOPE AND PHILOSOPHY

The AMA Computer Systems in Medicine Consultative Services Program is limited to activities related to the health care environment. Our services are directed to physician-centered organizations including solo physicians; group practices; clinics, hospitals; and medically related educational institutions, societies and government agencies.

Within an organization, the scope of our consultation will be established by the needs of the organization and the desires of the responsible professionals. Our capabilities extend to all major facets of computer applications in medicine, including the use of computers in clinical activities, medical records, administrative functions and ancillary services such as clinical laboratories and education.

While the major thrust of the Consultative Services Program will result from interest in the use of computers or computer related services, the major goal of the consultant is to provide recommendations for the most advantageous treatment of the particular situation; and that could mean manual methods as well as computer based methods. *The focus is the needs and objectives of the client, not the promotion of computerized solutions.*

We do not believe it is either appropriate or desirable for a consultant to make decisions for the client. Our role is to be a source of knowledge, expertise and objectivity which may not be otherwise available to the client. Our recommendations are based on the most complete and accurate information available to us and are specifically tailored to the needs and constraints of the client. Our recommendations should be considered exactly that — recommendations to be evaluated by the client's primary decision makers in the light of their unique understanding of their own environment.

Also, we do not believe in unnecessarily restricting the alternatives presented to a client. We will provide as many alternatives as we can identify that meet the requirements of the client's needs and environment. We will not, in the interests of efficiency, address ourselves to any alternative previously considered and rejected by the client unless additional events or infor-

mation affecting that alternative have intervened.

Regarding specific vendors or suppliers, it is our intention to provide as many qualified sources as *we know exist*. We will not exclude any vendor or supplier except if, in our judgment, they clearly do not provide a product or service that is applicable to the criteria and constraints of the environment.

## RESOURCES

The AMA computer Systems in Medicine Consultative Services Program in addition to the extensive resources of the American Medical Association in all aspects of health care, has significant expertise specifically in the application of computers to medicine.

Briefly, we have the following kinds of experience available among our people to draw upon and apply to our activities:

- Experience with a broad range of computing equipment from minicomputers to very large and sophisticated computer systems.
- Experience with batch systems; real-time, on-line systems; and interactive systems.
- Experience in all facets of health care computing including administrative systems, medical systems and laboratory systems.
- Experience in university oriented systems, administrative and academic.
- Experience in research — oriented computing and the administrative requirements of research.
- Experience in organizational analysis and management.

## ACTIVITIES

The Consultative Services Program has established expertise extending from general decision making on the utilization of computers in medicine to detailed systems design, programming and implementation of systems. However, we believe our expertise and resources are best utilized when applied to the basic issues affecting the success or failure of computeri-

zation in an organization. For that reason, we limit our consultation to activities such as: 1) needs analysis; 2) alternatives development; 3) specifications development; 4) proposal evaluation; 5) systems audits; 6) applications audits; and, 7) quality assurance.

1. Needs Analysis — Evaluation of the organization to determine functional requirements and constraints. This would include identification of the needs and objectives of the organization, present and projected workload, and points of potential disruption, bottleneck or inadequate levels of performance.
2. Alternatives Development — Formulation of alternative methods of operation based either on the results of needs analysis or a defined need of the client, evaluation of those alternatives based on acceptable criteria, and identification of the most appropriate alternative.
3. Specifications Development — Formulation of information on the operations targeted for alternative methods in sufficient detail to serve as the requirements section of a Request for Proposal (RFP). This RFP would be provided to appropriate vendors with the intent that they respond with a suggested system for achieving the requirements and the costs associated with that system.
4. Proposal Evaluation — Follows the distribution of RFP's and involves two phases. The first phase is to establish the criteria against which proposals will be evaluated. The second phase is the actual evaluation of proposals and a ranking of how well they satisfy the criteria.
5. Systems Audits — Evaluation of an existing system and all of the applications it handles to determine if actual operation meets or exceeds the initial criteria established as systems goals.
6. Applications Audits — Similar to a system audit except it is limited to a particular



application within a system.

7. Quality Assurance — Evaluation of an activity to determine if it is consistent with generally accepted principles and procedures for similar activities and will contribute to the overall objectives of the organization in an efficient and economical fashion. It is similar to an audit except that it is prospective rather than retrospective.

Other activities at the same general level of impact will be considered on an individual basis at the request of an existing or prospective client.

### METHODOLOGY

Our general approach consists of three relatively distinct phases of activity.

The initial phase is on-site analysis. In this phase, the consultant visits the client's facilities for first hand observation of the organization's procedures and information flow; to interview physicians and staff concerning their particular requirements and desires as well as their current methods of completing their tasks; and to identify the problems and potentials for improvement. At the conclusion of the on-site analysis the consultant will make a verbal report to the decision makers of the organization summarizing his initial findings and making tentative recommendations based on those findings.

The second phase is devoted to detailed analysis of the information collected during the on-site analysis; identification of specific problem areas and/or areas with opportunity for improvement; development of alternative methods of solving the problems and achieving the improvements; and selecting and justifying the recommended alternative.

The final phase consists of preparing the written report which is submitted as part of every engagement. This requires development of a summary of findings and recommendations; recording all pertinent observations; and specifying each recommendation with the supporting information, the other alternatives available and the expected results of implementing the recommendations.

### COSTS AND AVAILABILITY

The charge for AMA Consultative Services is

\$200.00 per day plus reimbursement of expenses for travel, lodging and meals incurred to complete the on-site analysis.

The \$200.00 daily fee has been established in order to partially recover the costs of this program from those who take advantage of the services.

The policy of the Consultative Services Program with respect to reimbursible expenses is to minimize the amount of expenses to those which are necessary and to make every effort to utilize the least expensive option available.

The minimum time for an on-site analysis is one day with the average being two to three days. The actual number of days depends on the size of the organization and the complexity of the activities being analyzed. A number of days approximately equal to that required for on-site analysis, will be spent at our offices doing detailed analysis of the data collected, formulating alternatives and preparing written recommendations. Therefore, the minimum fee would be \$400.00 and the average would be \$800-\$1200 plus out-of-pocket expenses.

The specific date for performing the on-site analysis is established by mutual agreement of the client and the consultant. The scheduling of available time will be handled by the AMA Consultative Services Program on a strict "first come, first serve" basis.

John A. Guerrieri, Jr.

Director, Consultative Services Program  
Department of Computer Systems in Medicine, Division  
of Medical Practice  
American Medical Association

Mr. Guerrieri's responsibilities include overall management and coordination of the Consultative Services Program in addition to serving as principal consultant. Mr. Guerrieri will provide consultation in the areas of: 1) identification and evaluation of the need for computer systems; 2) development of alternatives for achieving specified objectives; 3) development of specifications requirements for procurement of systems and/or services; 4) evaluation of vendor proposals; and 5) audit of systems and services to determine actual performance compared to expected performance.

Mr. Guerrieri has a B.A. degree in Mathematics from Northwestern University and an MBA degree in Quantitative Methods and Management from Loyola University of Chicago. He was awarded the Certificate

in Data Processing by the Institute for Certification of Computer Professionals on the basis of written examination.

Mr. Guerrieri has over 12 years of experience in computer-based information systems. During those years he functioned as a programmer, systems analyst, manager and consultant. He has experience on a variety of systems ranging from very large to minicomputer-based with special emphasis in on-line real-time and interactive systems spanning more than 10 years. He has experience with assembly languages as well as with COBOL, FORTRAN, RPG and MUMPS languages.

Mr. Guerrieri has experience in business, industrial and health care environments. His involvement with computers in the health care environment started in 1965 when he provided programming direction to several hospitals converting to IBM System 360's.

After a period of concentration in business and industrial applications, Mr. Guerrieri again became involved with health care organizations in 1969, in his role as Director of Professional Services for an information systems related professional association.

In that position, as well as in a subsequent position as Information Systems Manager for a hospital services organization, Mr. Guerrieri has provided consultation to a number of health care organizations seeking to automate recordkeeping functions. Emphasis was on the application of on-line real-time and interactive solutions to the automation of clinical as well as administrative medical information requirements.

Immediately prior to joining the American Medical Association, Mr. Guerrieri had responsibility for establishing the information systems function for a new medical services organization. This encompassed specification, design and implementation of hardware, software and data base requirement for: 1) a clinical laboratory including capture and maintenance of demographic financial, medical and laboratory data; and 2) an interactive time sharing organization providing a full range of computer services to health care organizations, including automated medical histories, creation and maintenance of medical records, patient and third party billing, other financial applications and various management reports.

## A N U N C I O S

### *URBANIZACION SAN FRANCISCO RIO PIEDRAS*

Atractiva residencia propia para oficina médico y/o laboratorios, próxima a centro comercial y colegios Santa María Reina y San Ignacio. Solar 1551.85 m<sup>2</sup>, 4,251 pies cuadrados de sólida construcción, 3 niveles, pisos terrazo integral, 5 dormitorios, 5 1/2 baños, habitación de servicio con baño, terraza galería, cocina equipada, aire central en las habitaciones, biblioteca, piscina, verja, rejas y sobre todo una localización privilegiada, excelentes condiciones de financiamiento. Véala sin compromiso mediante cita con Emma Cabañas, teléfonos 723-6796 y 722-6874 o Metropolitan Real Estate — teléfonos 790-1072, 790-1073 y 789-3736.

### *SE ALQUILA*

Alquilo local decorado, alfombrado y con aires acondicionados, para oficina médica propia para cualquier especialidad. El área es de aproximadamente 500 pies cuadrados con facilidades comunes a oficina de Pediatra y Laboratorio Clínico. Amplio estacionamiento. Está localizada en área de crecimiento, calle Paraná 1645 Paradise Hills, Cupey (entrada a la mayoría de las urbanizaciones de Cupey).

Para información llamar a los teléfonos: 764-8164 y 765-8592.

CONTRATISTA DESEA COMUNICARSE CON VARIOS DOCTORES QUE INTERESEN INSTALAR CLINICA SUBURBANA EN CENTRO COMERCIAL DE BAYAMON.

VENCEDOR DEVELOPMENT CORP.

Thomas R. Frame - 785-2150

## LISTA DE ANUNCIANTES


- |                          |                           |
|--------------------------|---------------------------|
| 1. BOEHRINGER INGELHEIM  | TORECAN                   |
| 2. BURROUGHS WELLCOME    | CODEINE ANAL., SEPTRA     |
| 3. CARNATION             | EVAPORATED MILK           |
| 4. MERCK SHARP & DOHME   | ALDOMET                   |
| 5. ROCHE LAB.            | BACTRIM, GANTANOL, VALIUM |
| 6. W. H. RORER           | ASCRIPITIN A/C            |
| 7. SMITH, KLINE & FRENCH | DIYAZIDE                  |
| 8. SYNTEX LAB.           | NEO-MULL-SOY              |
| 9. UPJOHN COMPANY        | MEDROL DOSEPAK            |

\*\*\*\*\*



What do you mean:  
You'd much rather  
play "doctor.?"





**"Little Boy Blue,  
come blow your horn,  
The sheep's in the  
meadow, the cow's  
in the corn..."**

Since cow's milk and corn are leading causes of food allergy among infants, NEO-MULL-SOY® formula doesn't contain either one. Other leading soy formulas do contain corn syrup. Next time recommend corn-free NEO-MULL-SOY formula first. Mothers like its milky whiteness. And now it's easier for them to find NEO-MULL-SOY formula, because it's more readily available at grocery and drug stores.



**NEO-MULL-SOY®**

Soy Isolate Formula

**The only leading soy formula  
that's milk-free AND corn-free.**

**SYNTEX**

SYNTEX LABORATORIES, INC.  
PALO ALTO, CALIFORNIA 94304

# Septra® vs Nitrofurantoin

Each tablet contains:  
80 mg trimethoprim and 400 mg sulfamethoxazole

## A new clinical

### **Efficacy: A draw.**

By randomized assignment, 149 patients received two Septra tablets b.i.d. and 140 received one 100 mg capsule of nitrofurantoin macrocrystals q.i.d. for 14 days. Eight days after therapy ended, 94% of patients treated with Septra had a clear culture vs 90% of those treated with nitrofurantoin macrocrystals.<sup>1</sup>

### **Laboratory changes: A draw.**

There was no significant difference in the incidence of laboratory changes except in one instance; a significantly larger proportion of patients on nitrofurantoin macrocrystals had decreased lymphocyte counts than did patients on Septra.<sup>1</sup> The significance of this change is not known. (For further details see page three of this advertisement.)

### **Clinical side effects: Advantage, Septra.**

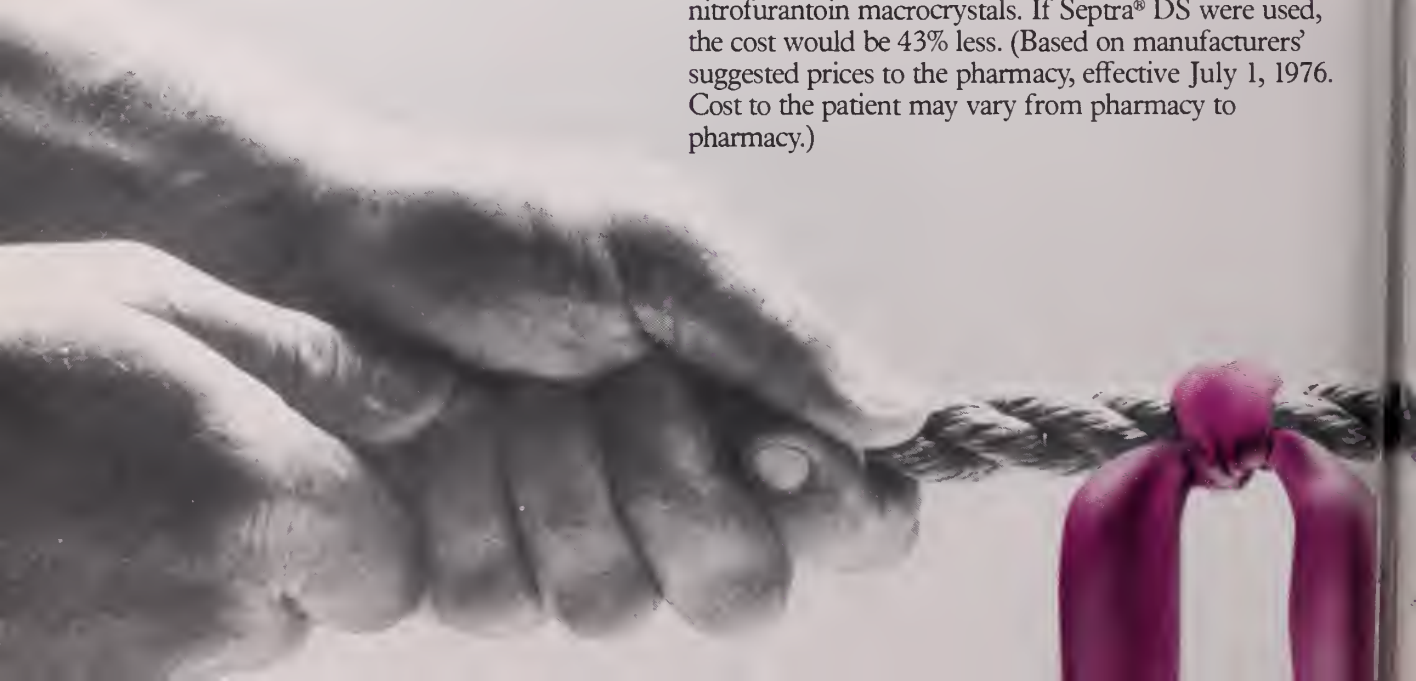
A significantly larger proportion of patients experienced side effects on nitrofurantoin macrocrystals (13%) than on Septra (6%).<sup>1</sup> (For further details, see chart on page three of this advertisement.)

### **Convenience: Advantage, Septra.**

To maintain effective antibacterial activity, Septra is taken just twice a day, while nitrofurantoin macrocrystals are taken four times daily. The Septra dosage schedule offers obvious advantages in terms of patient convenience and compliance.

### **Cost: Advantage, Septra.**

At the dosages used in this study, a course of therapy with Septra would cost 26% less than a course of nitrofurantoin macrocrystals. If Septra® DS were used, the cost would be 43% less. (Based on manufacturers' suggested prices to the pharmacy, effective July 1, 1976. Cost to the patient may vary from pharmacy to pharmacy.)



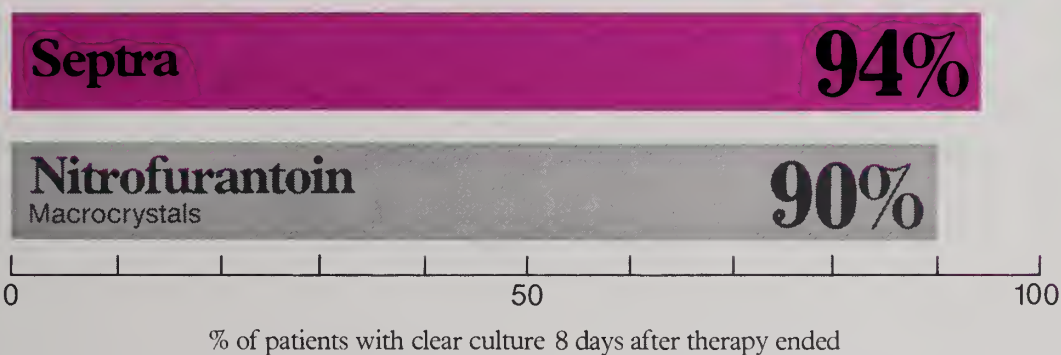


# Nitrofurantoin

Macrocrystals

## Confrontation

Results after 14-day course of therapy in 289 patients with recurrent urinary tract infections\*<sup>1</sup>



\*Due to susceptible strains of *E. coli*, *Klebsiella*, *Enterobacter*, *Proteus mirabilis* and other *Proteus* species. Criterion for infection—100,000 or more organisms/ml urine. Criterion for “clear culture”—1,000 or fewer organisms/ml urine.

# Septra<sup>®</sup> DS

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

**Double Strength Tablets.**

**The most economical form of Septra.**

See next page for prescribing information.





# Septra<sup>®</sup> vs Nitrofurantoin

Each tablet contains:

80 mg trimethoprim and  
400 mg sulfamethoxazole

Macrocrystals

## Clinical side effects: Advantage, Septra.

Side effect	Frequency <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
nausea	3	16
vomiting	1	9
anorexia	1	4
abdominal pain	—	2
diarrhea	—	4
headache	2	—
dizziness	—	1
diaphoresis	1	—
pruritus	2	1
vaginitis	1	—
maculopapular rash	1	1
rash	—	2
urticaria	2	—
	14	40

**Note:** All patients who originally entered the study described on previous pages were included in the evaluation for clinical side effects (192 patients received Septra, 191 received nitrofurantoin macrocrystals). Some patients experienced more than one side effect. See **Adverse Reactions** section below for other reactions that may be encountered.

## Laboratory changes: A draw.

Type of change	Drug administered	
	No. patients with change/total patients tested <sup>1</sup>	
	Septra	Nitrofurantoin macrocrystals
RBC ↓	14/141	14/141
Hemoglobin ↓	27/188	36/183
WBC ↑	3/188	3/183
" ↓	6/188	7/183
Bands ↑	3/183	3/176
" ↓	26/183	20/176
Hematocrit ↓	34/188	27/183
SGOT ↑	5/176	4/167
Basophils ↑	14/179	16/171
Neutrophils ↑	27/188	25/182
" ↓	3/188	6/182
Lymphocytes ↑	15/188	18/182
" ↓	11/188	21/182
Eosinophils ↑	14/179	8/177
Monocytes ↑	10/188	11/180
" ↓	23/188	23/180
Specific gravity ↑	1/187	—
" " ↓	—	1/177
Casts ↑	6/186	5/182
WBC/HPF ↑	9/190	13/185
RBC/HBF ↑	12/190	12/185
Bacteria ↑	9/189	11/183
" ↓	30/189	32/183
Crystals ↑	9/185	9/181

**Note:** Certain patients were not tested for some of the laboratory values listed above. Therefore, the chart specifies the total number of patients who completed the prescribed series of tests for each individual laboratory measurement.

**Indications:** Chronic urinary tract infections evidenced by persistent bacteriuria (symptomatic or asymptomatic), frequently recurrent infections (relapse or reinfection), or infections associated with urinary tract complications, such as obstruction. Primarily for cystitis, pyelonephritis or pyelitis due to susceptible strains of *E. coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris* and *Proteus morganii*.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37: 20527-20529, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted. At present, data are insufficient to recommend use in infants and children under 12.

**Precautions:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria,

serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for children under 12. Usual adult dosage: 1 Septra DS tablet or 2 Septra plain tablets or 4 teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	1DS tablet, 2 tablets or 4 teaspoonfuls (20 ml) every 24 hours
Below 15	Use not recommended

**Supplied:** Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—bottles of 60 tablets. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottles of 450 ml.

**Reference:** 1. Data on file, Medical Department, Burroughs Wellcome Co.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

Unlock arthritis pain  
and inflammation with  
the right combination!

# Ascriptin<sup>®</sup> A/D

Arthritic Doses



## Aspirin 325 mg.

Still the rheumatologist's  
anti-inflammatory analgesic drug  
of choice for the control of arthritis.

## Maalox<sup>®</sup> 300 mg.

Still the gastroenterologist's antacid  
of choice, providing dependable gastric  
protection at optimum dosage levels.

## Ascriptin<sup>®</sup> A/D

Now a better approach for salicylate control  
of arthritis with less gastric irritation  
(as illustrated by endoscopy\*).

\*Data on file, William H. Rorer Medical Department.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034





**We've been delivering for  
four generations--and still cost less.**

Carnation Evaporated Milk formulas have been raising strong, healthy babies since 1899—delivering the good, sound, natural nutrition newborns and infants thrive on. You see, Carnation Evaporated Milk has naturally occurring protein with all other

nutrients intact. You indicate vitamins, iron and carbohydrates to meet each baby's needs.

Importantly, a whole formula made with Carnation Evaporated Milk still costs new mothers less than any other. Carnation Evaporated Milk...for four generations. The babies under your care will thrive on it, too.



**FREE!** Send for sample copies of these informative patient oriented booklets: "Preparing Your Baby's Formula," "You and Your Contented Baby". Mail to: Carnation Company, GPO Box 682, San Juan, Puerto Rico 00936.

Name \_\_\_\_\_  
Address \_\_\_\_\_  
City \_\_\_\_\_  
State \_\_\_\_\_ Zip \_\_\_\_\_

Proximate analysis (per 100g): Moisture 73.7g;  
Fat 7.9g; Protein 7.0g; Ash 1.5g; Carbohydrate 9.9g;  
Calories 138; Vitamin A 320 IU; Vitamin D 79 IU.  
CARNATION® EVAPORATED MILK, CARNATION COMPANY  
LOS ANGELES, CA 90036.



**Upjohn**

The Upjohn Company, Kalamazoo, Michigan 49001

# Medrol<sup>®</sup> 4 mg Dosepak<sup>\*</sup> methylprednisolone, Upjohn

The explicit printed dosage instructions that accompany each Dosepak make it easy for the patient to understand and follow the dosage regimen.



## To relieve nausea and vomiting associated with

- postoperative recovery
- radiation therapy
- chemotherapy
- acute situations

(Contraindicated in pregnancy, severe CNS depression, comatose states and in patients who have demonstrated a hypersensitivity to phenothiazines.)

## Three dosage forms with the same 10 mg dosage strength:

**Tablets**—10 mg (thiethylperazine maleate, NF)



**Suppositories**—10 mg (thiethylperazine maleate, NF)



**Injection**—10 mg/2cc ampul (thiethylperazine maleate, NF) for IM use only.



# Torecan<sup>®</sup>

(thiethylperazine)

Still available in  
Puerto Rico



**Boehringer Ingelheim**

Boehringer Ingelheim Ltd.  
Elmsford, New York 10523

**Torecan<sup>®</sup>** (thiethylperazine)

Tablets, Suppositories and Injection

**Contraindications:** Severe CNS depression, comatose states, and in patients who have demonstrated a hypersensitivity to phenothiazines (e.g., blood dyscrasias, jaundice). Because severe hypotension has been reported after the intravenous administration of phenothiazines, this route of administration is contraindicated. The drug is contraindicated in pregnancy.

**Warnings:** Phenothiazines are capable of potentiating CNS depressants as well as atropine and phosphorous insecticides. The drug may impair mental and/or physical ability required in the performance of potentially hazardous tasks such as driving a car or operating machinery.

**Postoperative Nausea and Vomiting:** When used to control postoperative nausea and vomiting in patients undergoing elective surgical procedures, restlessness and postoperative CNS depression during anesthesia recovery may occur. Possible postoperative complications of a severe degree of any of the known reactions of this class of drug must be considered. Postural hypotension may occur after an initial injection, rarely with the tablet or suppository. Do not use with epinephrine in the treatment of drug-induced hypotension as phenothiazines may induce a reversed epinephrine effect. The most suitable vasoconstrictor agents are levarterenol and phenylephrine. The use of Torecan has not been studied following intracardiac and intracranial surgery. Not recommended for use in children under 12 years of age, or in nursing mothers since safety and efficacy have not been established.

**Precautions:** Convulsions and abnormal movements such as extrapyramidal symptoms have occurred. The varied extrapyramidal symptom complex is more likely to occur in young adults and children. Extrapyramidal effects must be treated by reduction of dosage or cessation of medication. For treatment of nausea and/or vomiting associated with anesthesia and surgery, the drug should be administered by deep intramuscular injection at or shortly before the termination of anesthesia.

**Adverse Reactions:** CNS convulsions, extrapyramidal symptoms such as dystonia, torticollis, oculogyric crisis, akathisia and gait disturbances, occasional cases of dizziness, headache, fever and restlessness have been reported. Drowsiness may occur initially on injection but is usually alleviated by a reduction in dosage. Dryness of the mouth and nose, blurred vision, tinnitus, sialorrhea and altered gustatory sensation. Peripheral edema of the arms, hands and face. Cholestatic jaundice, cerebral vascular spasm and trigeminal neuralgia have been reported occasionally. The following have occurred with phenothiazine derivatives and should be considered: agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia, pancytopenia, eosinophilia, leukocytosis, miosis, obstipation, anorexia, paralytic ileus, erythema, exfoliative dermatitis and contact dermatitis; jaundice, biliary stasis. Hypotension, rarely leading to cardiac arrest; ECG changes. Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonos, oculogyric crises, tremor, muscular rigidity, akinesia, some of which have persisted for several months or years especially in patients of advanced age with brain damage. Menstrual irregularities, altered libido, gynecomastia, weight gain; false positive pregnancy tests. Urinary retention, incontinence, fever, laryngeal edema and angioneurotic edema, asthma. Hyperpyrexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. ECG changes. While there is no evidence that ECG changes are in any way precursors of any significant disturbance of cardiac rhythm, sudden and unexpected deaths apparently due to cardiac arrest have been reported in a few instances in hospitalized psychotic patients previously showing characteristic ECG changes. A peculiar skin-eye syndrome, which is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea, has also been recognized as a side effect following long-term treatment. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported.

**Drug Interactions:** Phenothiazines are capable of potentiating CNS depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorous insecticides. The drug may induce a reversed epinephrine effect on occasion.

For complete details, please see full prescribing information.





# ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

OCT 6 1977

BOLETIN

THE FRANCIS A. COUNTWAY



VOL. 69 AGOSTO 1977 NO. 8



# A character all its own.



Valium (diazepam) is a benzodiazepine with a character all its own.

Pharmacologically, it has been described as more potent mg-per-mg than other available anxiolytic benzodiazepines. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> (diazepam)<sup>Ⓢ</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.


**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



**In reflux  
esophagitis, if  
he could sleep  
standing up...  
any antacid  
might do**

**Camalox<sup>®</sup>**

(magnesium and aluminum hydroxides with calcium carbonate)

**increases lower esophageal sphincter pressure  
to prevent acid reflux from occurring nocturnally  
when the patient is horizontal.<sup>1</sup>**

**Camalox...the high-potency, long-lasting  
antacid that stands up even when the patient  
lies down.**

1. Higgs, R.H., Smyth, R.D., and Castell, D.O., Gastric Alkalinization—  
Effect on Lower-Esophageal-Sphincter Pressure and Serum Gastrin,  
The New Engl. J. of Med., 291: 486-490, 1974.



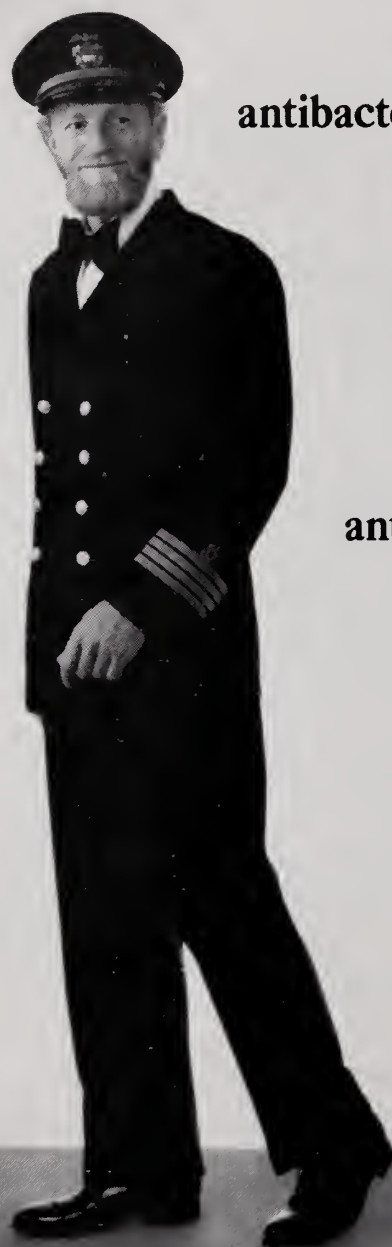
**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034

**anti-inflammatory**

**antipruritic**

**antibacterial**

**antifungal**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform®-Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; urticaria; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; Intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Use in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/6870 17

## Vioform®- Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

# ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial

Fundado en 1903

Volumen 69

Agosto 1977

Número 8

## JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bermúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

## Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

## Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

## Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Fibrosis Quística en Puerto Rico .....	251
José E. Sifontes, MD, Frank Rodríguez Pedro Mayol, MD, Rogelio Menéndez, MD Efraín Alicea, MD y Wilfredo Vélez, MD	
Acute Pre-Infarction Angina .....	258
Pablo I. Altieri, MD	
Dantrolene Sodium: An effective Therapeutic Agent for the Treatment of Spasticity in Children .....	263
José M. García Castro, MD	
Mycotic Pulmonary Artery Aneurysms: A Rare Cause of Fatal Hemoptysis .....	266
Hernán D. Giraldo, MD and José Ramírez Rivera, MD	
Polycystic Liver Disease: Case Report .....	272
A. H. Sarmiento, MD, A. E. Lanaro, MD and D. Vázquez, MD	
Brief Communication — Bleeding Duodenal Ulcer in a Patient Taking Slow-Releasing Potassium Tablets .....	276
Pablo I. Altieri, MD, Carmelo Herrero, MD Rómulo Suero, MD and Armando Ortiz, MD	
Noticias .....	277

PORTADA — BAHIA DE SAN JUAN  
(Cortesía del Banco Gubernamental de Fomento)

## FIBROSIS QUÍSTICA EN PUERTO RICO

José E. Sifontes, MD, Frank Rodríguez, MD, Pedro Mayol, MD, Rogelio Menéndez, MD  
Efraín Alicea, MD y Wilfredo Vélez, MD

El propósito de este trabajo es describir a grandes rasgos las características de la fibrosis quística en los niños puertorriqueños. Se considera de importancia hacerlo ya que escasea la información disponible sobre esta enfermedad en las áreas tropicales y podría ser de interés describir la frecuencia, los criterios de diagnóstico y las manifestaciones clínicas de la enfermedad según se presenta en el trópico.

### Materiales y Métodos

Se revisaron los expedientes de los pacientes atendidos en el Centro de Fibrosis Quística del Hospital Universitario de Niños de Puerto Rico durante los años 1973 a 1976. En estos pacientes se hizo el diagnóstico de la enfermedad a base de las manifestaciones clínicas principalmente enfermedad pulmonar crónica, trastor-

nos digestivos y el aumento en las cifras de cloruro del sudor sobre 60 meq por litro. Estamos utilizando el método de iontoforesis de Gibson y Cooke (1) \*. Se descartaron otras causas de aumento en el cloruro del sudor. Se estudiaron las cifras de CI del sudor en 554 niños puertorriqueños normales y se verificó que éstas nunca sobrepasaban 59 meq/l. (Tabla I). En la evaluación clínica de los enfermos se utilizaron los criterios que aparecen en la Tabla II. Estos son los recomendados por Shwachman y Kulczycki (2) traducidos y modificados por nosotros (3).

### Resultados

Entre el 1973 y 1976 se atendieron en el Centro de Fibrosis Quística de Puerto Rico 22 pacientes provenientes de una población de alrededor de 3 millones de habitantes. Nuestro centro es el único en Puerto Rico y en el mismo, entre 1967 y 1975, se diagnosticaron 33 pacientes. Cuatro eran norteamericanos. Los 29 puertorriqueños representan una incidencia de 2 a 3 pacientes nuevos por año. El número de recién nacidos vivos en Puerto Rico es de alrededor de 69,000 por año. Hemos estimado a base de la experiencia con autopsias\*\* que,

---

*Del Centro de Pediatría Pulmonar, Sección de Neumología Pediátrica, Departamento de Pediatría, Hospital Universitario de Niños de Puerto Rico.*

*Preparado con la ayuda de donativos de la Cystic Fibrosis Research Foundation y para el programa "Desarrollo de Personal para el Cuidado Pediátrico Pulmonar" del "Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration, Maternal and Child Health, Grant No. 950".*

*Ponencia para la Reunión Anual Pediátrica de la Fundación Macy, Santo Domingo, República Dominicana, Marzo 1977. (Tenth Annual Meeting of Leaders of Macy-Supported Programs in Latin America and the Caribbean).*

---

\* - Antes de junio de 1976 se usó el Lancer Cystic Fibrosis Analyzer, Sherwood Mo. EUA.

---

\*\* Comunicación personal de la Dra. Pilar Aliaga de la Sección de Patología Pediátrica de nuestra Escuela de Medicina: 1 caso por año en las autopsias pediátricas del Centro Médico de Puerto Rico de 1967 a 1975. Estimamos que esta cifra representa alrededor del 20 por ciento de la experiencia en Puerto Rico.



TABLA I  
CIFRAS DE CLORURO DEL SUDOR DE NIÑOS PUERTORRIQUEÑOS NORMALES  
N = 554 (53 POR CIENTO VARONES)

Edad (años)	Cl meq / litro	
	Cifras Máximas	Cifras Promedio *
< 1	48	24
1	42	25
2	42	26
3	56	26
4	54	26
5	54	30
6	38	25
7	43	24
8	58	32
9	50	32
10	42	26
11	34	27
12	48	26

\* Fleisher y González-Lebrón (Bol. Asoc. Med. P. Rico 61:17, 1969) informaron en 67 niños cifras de Cl de 18 a 26 meq/l. Nuestra serie más reciente utilizando el método de Gibson y Cooke arroja cifras un poco más bajas que las que se presentan en esta tabla.

probablemente, 5 lactantes afectados por la fibrosis quística fallecen sin haberse hecho el diagnóstico. Utilizando estas cifras estimamos que la incidencia de fibrosis quística en Puerto Rico debe ser de alrededor de uno por ocho mil recién nacidos.

Las manifestaciones clínicas de nuestros pacientes fueron principalmente pulmonares y digestivas. (Tablas III y IV). El 31 por ciento eran varones.

Los trastornos pulmonares se presentaron en todos los pacientes y consistieron en neumonías recurrentes, atrapamiento de aire, atelectasias, bronquiectasias, quistes y abscesos.

Los trastornos digestivos se manifestaron en 21 pacientes por diarrea, desnutrición, pro-

lapso rectal y detención del crecimiento y desarrollo.

Un paciente presentó trastornos pulmonares sin síntomas digestivos.

Cuatro de 22 pacientes (2 varones y 2 hembras) fallecieron: Dos a los 21 años, una a los 17 y otra a los 2 años. Sobreviven 18 o sea el 82 por ciento. La edad de éstos es de 2 a 17 años. Seis (33 por ciento) son menores de 6 años; diez (55 por ciento) son de 6 a 12 años y 4 (22 por ciento) son de 13 a 17 años. El 66 por ciento (12/18) de los sobrevivientes son del sexo femenino.

La puntuación clínica demostró enfermedad severa en 4 (22 por ciento) de los sobrevivientes; moderada en 4 (22 por ciento);

TABLA II  
EVALUACION CLINICA DE FIBROSIS QUISTICA\*

Calificación	Puntuación	Actividad General	Exploración Física	Nutrición	Radiografías
Excelente	25	Normal, Plena	Normal	Sobrepercentila 25; musculatura normal	Normales
Buena	20	Asiste a la escuela pero se cansa al finalizar el día	Tose raras veces. Pulmones claros Enfisema mínimo.	Percentila 15-25, musculatura regular	Acentuación de la trama y enfisema mínimo.
Leve	15	Asistencia a la escuela regular; descanso espontáneamente y se cansa fácilmente	Tose de vez en cuando. Taquipnea leve. Enfisema leve. Gruesos ruidos respiratorios y raras veces estertores o dedos hipocráticos.	Sobre la percentila 3: musculatura débil y reducida.	Leve enfisema. Acentuación de la trama. Focos atelectáticos.
Moderada	10	No asiste a la escuela. Disnea con caminatas cortas. Descansa mucho.	Tose frecuente y productiva. Retracciones. Enfisema moderado. Estertores. Dedos hipocráticos más acentuados: 2 - 3 +	Bajo percentila 3. Musculatura más débil y reducida.	Enfisema moderado. Areas atelectáticas diseminadas. Bronquiectasia mínima.
Grave	5	Ortopnea. Limitado a silla o cama.	Accesos severos de tos, taquipnea, alteraciones pulmonares extensas. Puede tener fallo cardíaco derecho. Dedos hipocráticos 3 - 4 +	Desnutrición avanzada. Prolapso rectal.	Alteraciones extensas, atelectasia lobar y bronquiectasias.

\*Modificada de "Guide to Diagnosis and Management of Cystic Fibrosis", pp. 94-95 (1971).

Una puntuación de 100 es la del paciente normal; sobre 85 excelente; de 71 a 85 buena; de 56 a 70 leve; de 41 a 55 moderada y menor de 40 grave. Esta puntuación generalmente está acompañada de cifras arteriales de  $PCO_2$  mayores de 45 mm. de Hg y de  $PO_2$  menores de 50 mm. de Hg. Estos enfermos deben vigilarse cuidadosamente para diagnosticar cor pulmonale a tiempo. (J. Pediat. 78: 794, 1971).

TABLA III  
MANIFESTACIONES CLÍNICAS  
SOBREVIVIENTES

Nombre	Sexo	Caso No.	Edad al Diag- nosticarse (Años)	Edad en Diciembre 1976 (Años)	Puntuación Clínica en Diciembre de 1976	Manifestaciones Clínicas	
						Pulmonares	Digestivas
C.G.G.	F	1	4	17 1/2	90	X	No
A.C.O.	F	2	6	17	90	X	X
O.R.M.	M	4	4	16	40	X	X
L.M.R.	F	6	10	14	90	X	X
B.T.V.	F	7	3/12	12	20	X	X
J.R.V.	M	8	5	10 1/2	80	X	X
O.M.P.	F	9	3	10 1/2	40	X	X
L.S.R.	F	11	5 1/2	9 1/2	60	X	X
A.A.N.	M	12	1	8 1/2	40	X	X
L.W.	F	14	3/12	8	70	X	X
N.T.D.	F	15	4 1/2	8	50	X	X
O.G.P.	F	16	7 1/2	8	70	X	X
B.P.D.	F	18	3 1/2	6 1/2	90	X	X
R.R.L.J.	F	19	3	6 1/2	50	X	X
W.F.	M	20	4 1/2	5 1/2	50	X	X
J.R.I.J.	M	22	5/12	3 1/2	80	X	X
D.S.D.	F	23	5/12	3	50	X	X
E.D.R.	M	24	8 1/2	2 1/2	70	X	X

leve en 4 (22 por ciento); buena en 2 (11 por ciento) y excelente en 4 (22 por ciento). Esta puntuación se había mantenido estable desde que se hizo el diagnóstico hasta diciembre de 1976 en todos los casos menos tres que empeoraron. El intervalo entre el comienzo del tratamiento y diciembre de 1976 aparece en la Tabla V.

El tratamiento de estos pacientes incluyó dieta adecuada, enzimas pancreáticas por la vía oral, fisioterapia, antimicrobianos cuando estos eran necesarios y la hospitalización de

pacientes que desarrollaron dificultad respiratoria u otro trastorno importante. En la Tabla VI se presentan los pormenores de la terapéutica utilizada. Las complicaciones más importantes que hemos encontrado aparecen en la Tabla VII.

#### Discusión

La incidencia de fibrosis quística en Puerto Rico parece ser más alta que la que se encuentra



TABLA IV  
MANIFESTACIONES CLINICAS  
FALLECIDOS

Nombre	Sexo	Caso No.	Edad al Diagnos- ticarse (Años)	Edad al Morir ( Años)	Causa de Muerte	Manifestaciones Clínicas Predominantes	
						Digestivas	Pulmonares
J.J.C.	M	19	4	21	Desconocida	X	X
R.S.	M	20	7	21	Hemoptisis	X	X
R.H.	F	21	13	17	Insuficiencia Respiratoria	X	X
S.A.	F	22	4/12	2	Insuficiencia Respiratoria	X	X

TABLA V  
AÑOS DE SUPERVIVENCIA DESPUES DE COMENZADO EL TRATAMIENTO

Años	Número de Pacientes
1	1
1 1/2	2 (1 falleció)
2 1/2	1
3	2
3 1/2	2
4	3 (1 falleció)
5 1/2	1
7	2 (1 falleció)
7 1/2	2
8	1
11	1
12	2
13 1/2	1
14	1 (falleció)

en los emigrantes de Paquistán en Inglaterra (1:10000), los italianos (1:15000), los orientales de Estados Unidos (1:90000) y en los negros norteamericanos (1:17000). Es, probablemente,

más baja que la que se encuentra en los caucásicos de los Estados Unidos y otros países nórdicos (1:620 a 1:3800) exceptuando la de Suecia y parte de la Unión Soviética Europea que infor-

## TABLA VI

## Tratamiento:

1. Dieta: *baja en grasa; alta en carbohidratos y proteínas.*
2. Suplementación de sal: *no ha sido necesaria en nuestros pacientes.*
3. Enzimas pancreáticas: *gránulos; Cotazyme; Viokase; Kuzyme H P.*
4. Tienda de nebulización: *no se ha usado.*
5. Terapéutica inhalatoria: *inhalaciones de neosinefrina y solución salina normal con "propylene glycol" y antibióticos hasta 1973.*
6. Drenaje postural: *consideramos ésta la terapéutica por excelencia; por lo menos 2 veces al día aunque la afección pulmonar sea mínima; se entrena a las madres y padres y cuando vienen a cita los supervisa la terapeuta.*
7. Antibióticos: *se utilizan en pacientes ambulatorios; se administran cuando desarrollan neumonía, hemoptisis, fiebre, anorexia, pérdida de peso o leucocitosis. Comenzamos con una, dos o las cuatro siguientes: oxacilina, tetraciclina, sulfisoxazole o cefalosporinas; luego modificamos la terapéutica de acuerdo con la sensibilidad de los microorganismos cultivados.*
8. Hospitalizaciones: *cuando el paciente no responde a tratamiento oral y la fisioterapia con percusión y vibración intensa (por lo menos cuatro veces al día). Se hospitalizan por un término no menor de 15 días y se tratan, en general, con gentamicina 5 mg/kg y carbenicilina 300 a 400 mg/kg por la vía endovenosa.*
9. Expectorantes y broncodilatadores: *aquellos pacientes con sibilancias, broncorrea intensa o ambas se tratan con teofilina y guayacolato por períodos de 1 a 2 meses.*
10. Andrógenos: *se utilizan solamente en casos muy deteriorados (2 pacientes) cuando tienen anorexia marcada, pérdida de peso y afecciones pulmonares severas; han sido de gran utilidad (0.1 mg/kg/día, oral de "oxandrolone" - Anavar, de Searle - por 7 a 14 días).*

man cifras parecidas a la de Puerto Rico (1: 8000) (4).

Las manifestaciones clínicas de la fibrosis quística en Puerto Rico presentan algunas diferencias cuando se comparan con las descritas en otros países. La postración por hipertermia no la hemos observado. La alta humedad relativa que caracteriza el clima puertorriqueño hace innecesaria la terapéutica en el hogar con tiendas humectantes. La temperatura de Puerto Rico raras veces baja de 18° C o sobrepasa 35° C. La cifra promedio es 26° C. El porcentaje de humedad nocturna es de 80 por ciento a 95 por ciento y diurna de 45 por ciento a 85 por ciento.

La evolución de la enfermedad y sus complicaciones parece ser más benigna en los pacientes puertorriqueños. Pero la esperanza de vida y la supervivencia, hasta ahora, parecen comparables a los informados por otros centros de fibrosis quística. Hemos encontrado una mortalidad que sigue una tendencia más alta que la observada en los niños de la raza negra en Cleveland, pero quizás más baja que la de los blancos de la misma ciudad (4). El número de casos que hemos evaluado es insuficiente para hacer afirmaciones contundentes. Para hacer esto necesitamos observación ulterior de nuestros casos a más largo plazo con evaluaciones de la función pulmonar y de los aspectos sicosociales del

TABLA VII

Complicaciones \*:

<i>Prolapso rectal</i>	- 1 paciente
<i>Neumotorax</i>	- 2 pacientes, 4 episodios
<i>Hemoptisis masiva</i>	- 1 paciente, murió durante el episodio
<i>Hemoptisis leve</i>	- frecuente cuando tienen infección; es una indicación para el uso de antibióticos
<i>Ileo meconial</i>	- 0
<i>Postración por calor</i>	- 0
<i>Obstrucción intestinal</i>	- 0
<i>Pólipos nasales</i>	- 0
<i>Las bronconeumonías, bronquiectasias y neumonías recurrentes las consideramos parte del cuadro clínico y no complicaciones. Los cultivos de esputo demuestran principalmente pseudomonas; no la hemos podido erradicar.</i>	

\* Antes del 1973 observamos otras complicaciones de importancia, tales como íleo meconial (3 casos), anasarca (1 caso), cirrosis hepática (1 caso), diabetes mellitus (1 caso), cor pulmonale (1 caso) y obstrucción intestinal (1 caso). (Referencias 5 y 6).

desarrollo de nuestros pacientes (7).

### Resumen y Conclusiones

La incidencia de la fibrosis quística en Puerto Rico es, probablemente, más baja que la que se informa en la mayoría de los países nórdicos y más alta que la que se encuentra en los orientales y los negros. Las características de la enfermedad y su evolución parecen ser menos severas que las de otros países del norte. La terapéutica humectante en el hogar y la administración de sal no han sido necesarias en Puerto Rico.

### Referencias

1. Gibson, L. E. y Cooke, A.: Test for concentration of elec-

- trolites in sweat in cystic fibrosis of the pancreas utilizing pilocarpine iontophoresis. *Pediatrics* 23: 545, 1959.
2. Shwachman, H. y Kulczycki, L. L.: Long-term study of one hundred-five patients with cystic fibrosis. *Amer. J. Dis. Child* 96: 615, 1958.
  3. Sifontes, J. E., Mayol, P. M., Rodríguez-Martínez, F. y Valcárcel, M.: *Neumología Pediátrica*, Recinto Universitario de Ciencias Médicas, Universidad de Puerto Rico, Library of Congress Cat. Card No. 73-92921, 1974.
  4. Wood, R. E., Boat, T. F. y Doershuk, C. F.: Cystic Fibrosis- State of the Art. *Amer. Rev. Resp. Dis.* 113: 833, 1976.
  5. Mayol, P. M.: Experiencia clínica sobre la fibrosis quística de Puerto Rico. *Memorias del Noveno Congreso Latinoamericano de Pediatría*, Vol. 2 p. 323, junio 1970.
  6. Mayol, P. M., Valcárcel, M. y Aliaga, P.: Obstrucción intestinal neonatal asociada con fibrosis quística, *Bol. Asoc. Med. P. Rico* 63: 92, 1971.
  7. Mangos, J. A. y Talamo, R. C.: Cystic Fibrosis - Projections into the future. An international conference held at the Israel Academy of Science and Humanities. Jerusalem, Israel, May 1976. Stratton Intercontinental Book Corporation, New York 10016.



## ACUTE PRE-INFARCTION ANGINA

Pablo I. Altieri, MD

**Abstract:** Three patients with acute pre-infarction angina are described. We discuss the hemodynamic and angiographic findings. All patients showed high grade obstruction of the left anterior descending or main trunk of the left coronary artery. It is our opinion that patients with preinfarction angina should undergo coronary angiography and surgical management should be entertained if severe involvement is found.

**Abstracto:** Tres pacientes con angina de pre-infarto aguda son descritos. Discutimos los hallazgos hemodinámicos y angiográficos. Es nuestra opinión que pacientes con angina de preinfarto aguda deben ser estudiados con angiografía coronaria, y el manejo quirúrgico está indicado si se encuentran lesiones severas en una de las coronarias principales.

There has been great interest in the management of patients with preinfarction angina due to the fact that the optimal management of this group of patients is not known.

Most of the reports dealing with this syndrome describe a group of patients with chronic,

stable angina, who develop a changing pattern of symptoms accompanied by transient electrocardiographic changes. Less importance has been given to a group of patients without any previous history of heart disease or chest pain, who presents with pre-infarction angina as the first manifestation of the disease. We prefer to describe this group of patients as having "acute pre-infarction angina".

It is the purpose of this report to describe the clinical and angiographic findings in three patients with acute pre-infarction angina.

### Materials and Methods

In reviewing our group of patients with pre-infarction angina we found three patients whose presentation was the syndrome of acute pre infarction angina. We adhere very strictly to the definition of pre-infarction angina which is described in Table I. All three patients had left heart catheterization and coronary angiography using the Judkins technique. Left ventricular cineangiography was performed in the 30° RAO position using 36-40 ml of hypaque injected during a 2-3 second interval. The left ventricular volumes and ejection fraction were determined by the area-length method (1, 2, 3). The dp/dt was measured using an R-C differentiator via fluid filled catheters. Atrial pacing was done in one patient.

### Results

Table II presents the clinical and electrocardiographic findings of the patients presented. All of them complained of chest pain at rest. The only risk factor was smoking. Physical examination was normal in one patient and in

---

*From the Division of Cardiology, University of Puerto Rico Medical School, Rfo Piedras, Puerto Rico.*

*Address for reprints: Pablo I. Altieri, MD, Director Cardiovascular Laboratory, University Hospital, P. R. Medical Center, Hato Rey, Puerto Rico.*

TABLE I  
DEFINITION OF PRE-INFARCTION ANGINA

1. *Ischemic cardiac pain consistent with unstable angina.*
2. *Transient electrocardiographic changes recorded during at least one episode of pain - change in the ST segment or T wave returning to control levels within 24 hours after onset of changes.*
3. *No new Q wave on the electrocardiogram.*
4. *No changes in serum enzymes (CPK, SGOT, SGPT, LDH over a 24 hour period).*

TABLE II  
CLINICAL MANIFESTATIONS OF PATIENTS  
WITH ACUTE PRE-INFARCTION ANGINA

<i>Sex</i>	<i>Age</i>	<i>Symptoms</i>	<i>Risk Factors</i>	<i>Physical Examination</i>	<i>Electrocardiogram Finding</i>	<i>Treatment</i>
<i>Male</i>	<i>47</i>	<i>chest pain at rest</i>	<i>smoking</i>	<i>S<sub>4</sub> gallop</i>	<i>3mm ST depression V<sub>3</sub>-V<sub>6</sub></i>	<i>Propranolol and Nitroglycerin</i>
<i>Male</i>	<i>41</i>	<i>chest pain at rest</i>	<i>smoking</i>	<i>S<sub>3</sub> gallop</i>	<i>T wave inversion V<sub>3</sub>-V<sub>6</sub> V. T.</i>	<i>Propranolol nitroglycerin and vein bypass</i>
<i>Male</i>	<i>38</i>	<i>chest pain at rest</i>	<i>smoking</i>	<i>Normal</i>	<i>T wave inversion V<sub>2</sub>-V<sub>6</sub></i>	<i>Propranolol and nitroglycerin</i>

one patient and in the other 2 patients gallops were heard intermittently (S<sub>3</sub> , S<sub>4</sub> gallops).

The electrocardiograms were abnormal during episodes of chest pain. Two patients showed T wave inversion, the other prominent ST-segment depression (the patient with main stem lesion). One patient had repeated episodes of ventricular tachycardia.

The initial treatment in all patients consisted of continuous electrocardiographic monitoring, sublingual nitroglycerin as needed, and high doses of propranolol (up to 350 milligrams daily). All of them were catheterized after their symptoms subsided with medical therapy. One patient had a saphenous vein aorto-coronary bypass to the left anterior descending artery,

TABLE III  
HEMODYNAMIC AND ANGIOGRAPHIC FINDINGS OF  
PATIENTS WITH ACUTE PRE-INFARCTION ANGINA

EDP	DP/DT	E.F.	VENTRICULOGRAM	CORONARY ARTERIES
12		.72	Normal	90 percent main stem LCA
16 post = 25 pacing	2000	.59	Hypokinetic antero-apical segments	90 percent LAD
10 post = 25 angiogram	1813	.60	Hypokinetic antero-apical segments	100 percent LAD

EDP = End-diastolic pressure

dp/dt = Rise in intraventricular pressure

E. F. = Ejection Fraction

LCA = Left Coronary Artery

LAD = Left Anterior Descending

one was not considered a candidate for surgery and the other died during cardiac catheterization. This patient had a main stem lesion and eventually was going to be treated with a coronary bypass. Table III shows the hemodynamic and angiographic findings of the three patients. The end-diastolic pressure was elevated in one patient, but it increased abnormally in the other two after atrial pacing and ventricular angiography. The dp/dt was normal in two patients, in the other patient it wasn't recorded. Three patients had normal values for ejection fraction, although two of them showed hypokinetic areas (antero-apical segments) which corresponded to the site of the coronary lesion.

All patients reported showed high grade obstruction of the left anterior descending or main trunk of the left coronary artery.

#### Discussion

The management of pre-infarction angina

presents a vexing problem. Some investigators have proposed that the management of this group of patients is strictly surgical (4), while other have reported that the mortality is less or the same in medically treated patients (5). Lambert et al (6) reported 48 surgically treated cases of pre-infarction angina with only 2 intra operative deaths. They concluded that the operative mortality was less than the 20 percent incidence of acute infarction in the medically treated group.

Conti (5) have reported that there is no difference in mortality in both groups. On the other hand Favaloro (4) reported 18 patients with pre-infarction angina, treated surgically with only 2 deaths. He concluded that surgery is the treatment of choice. He stressed the importance of early angiographic studies and aorto-coronary bypass surgery. Cheanvechai (8) reported the Cleveland clinic results. The mortality in 63 patients with this syndrome was 6 percent, 92 percent of patients were asymptomatic



at 1 year follow-up. Johnson (9) and his associates reported a zero hospital mortality and no post operative infarctions in 44 patients.

Most studies have indicated, that pre-infarction angina is associated with a greater risk of infarction and death than stable angina, but the difference is not striking. In the Myocardial Infarction Research Unit, the mortality rate of pre-infarction angina is 7.7 percent at 1 year (7). In the Veterans Administration Cooperative study, the overall mortality of medically treated patients with stable angina was 8 percent at one year (10). At the Palo Alto Veterans Administration Hospital, there was no difference in mortality between the pre-infarction and stable angina treated medically (10).

Several investigators have reported that perioperative infarction in stable and pre-infarction angina is about 00 percent (10, 11, 12). Because a principal reason for surgical intervention is the prevention of infarction; it is disturbing that surgery is so frequently accompanied by infarction.

Interestingly enough they don't pay much attention in dividing the patients in the 2 different groups of pre-infarction angina (Table IV).

TABLE IV

SUBGROUPS OF PRE-INFARCTION-ANGINA

---

1. Angina of recent origin.

2. Chronic angina with a changing pattern.

---

In our opinion, it is extremely important to classify them in the 2 subgroups and adhere strictly to the definition, especially the lack of appearance of Q waves and no enzyme changes.

Some investigators stress or believe that pa-

tients with known chronic coronary disease with a changing pattern should be treated conservatively with propranolol and nitroglycerine. It is our opinion, that in patients having an acute pre-infarction syndrome, a high grade stenosis of one of the main coronary arteries must be considered and angiography should be done. It is recognized that 8 to 12 percent of patients with pre-infarction angina may have left main stem coronary lesion (13). It is now also recognized that this lesion is a serious one with poor prognosis and one in which surgical management is preferable to medical treatment. Again we think that we should try to stabilize the patients with high doses of propranolol and nitroglycerin, and then operate on an urgent but not emergency basis, since studies of pre-infarction angina reveal a small number of early hospital deaths and infarction (14, 15).

The use of propranolol in patients with coronary artery disease have been increasing lately. This agent tends to decrease myocardial oxygen consumption and by doing this reduce the extent of ischemic myocardial injury or even reduce infarct size (16). In our patient (number 3) with complete obstruction of the left anterior descending artery proximal to the first septal perforator we may have prevented a transmural infarction by the use of high doses of propranolol. He was admitted with classic finding of pre-infarction angina. He was started on propranolol, nitrates and was catheterized 3 days after admission. The ventriculogram showed hypokinesis of the antero-apical wall and 100 percent obstruction of the left anterior descending artery at its origin. The electrocardiogram after the symptoms subsided, reverted to a completely normal tracing. It is interesting to propose that the use of propranolol prevented a catastrophic event. After the patient was discharged he continued completely asymptomatic and returned to work.

The catheterization findings in this group of patients showed normal ejection fraction, although 2 patients showed hypokinetic areas. This is in contrast to the group reported by

Chatterjee who showed severe depression of left ventricular function with critical stenosis of the left coronary artery (17).

We had one death during catheterization. This was the patient with a main stem lesion and a small right coronary artery. This patient developed cardiogenic shock after the third injection in the left coronary. On autopsy, we were unable to detect a myocardial infarction, even after special stains were done. The explanation of this problem can be as follows: Coronary flow is only reduced during catheterization, if there is a high grade stenosis of the coronary artery being catheterized. If flow is reduced in the left coronary artery and the right coronary artery is small, the contrast material may stay too long in the sinusoids depressing the myocardium and producing a pump failure. It is important to discuss that the risk of death of coronary angiography has now been substantially reduced and appears to be no greater than that of patients with stable angina. The Palo Alto Veterans Administration Hospital reported no mortality and only one non-fatal infarct (10).

Patients with acute pre-infarction angina should be treated aggressively with early angiography; if possible, after the patient's symptoms are eliminated by propranolol and nitroglycerin. These patients may show a high grade stenosis of one of the main coronary arteries and a coronary bypass will probably prevent a massive myocardial infarction.

## References

1. Sandler, H., Dodge, H. T.: The use of single plane angiograms for the calculation of left ventricular volume in man. *Amer Heart J* 75: 325, 1968.
2. Kasser, I. S., Kennedy, J. W.: Measurement of left ventricular volumes in man, with single plane cineangiocardiology. *Investigative Radio* 14: 83, 1969.
3. Kennedy, J. W., Trenholme, S. E., Kasser, I. S.: Left ventricular volumes and mass from single plane cineangiocardiology. A comparison of antero posterior and right anterior oblique method. *Amer Heart J* 80: 343, 1970.
4. Favaro, R. G., Effler, D. B., Cheanvechai, C., Quint, R. A. and Sones, F. M.: Acute coronary insufficiency (impending myocardial infarction and myocardial infarction). Surgical treatment by the saphenous vein graft technique. *Amer J Cardiol* 28: 598, 1971.
5. Conti, C., Gilbert, J., Hodges, M.: Unstable angina pectoris: randomized study of surgical US medical therapy (National Cooperative Unstable Angina Pectoris Study group) (abstr). *Amer J Cardiol* 35: 129, 1975.
6. Lambert, C. J., Adam, M., Geisler, G. F., Verzosa, E., Nazarian, M., Mitchell, B. F.: Emergency myocardial revascularization for impending infarctions and arrhythmias. *J of Thorac and Cardiovasc Surg.* 62: 522, 1971.
7. Conti, R., Brawley, R., Pitt, B., Ross, R.: Unstable angina: morbidity and mortality in 57 consecutive patients evaluated angiographically. *Amer J Cardiol* 31: 127, 1973.
8. Cheanvechai, C., Effler, D. B., Loup, F. I., Oreves, L. K., Sheldon, W. C., Razari, M., Sones, F. M.: Emergency myocardial revascularization. *Amer J Cardiol* 31: 125, 1973.
9. Auer, V. E., Johnson, W. D., Flemma, R. J., Tector, A. J., Lepley, D.: Direct coronary surgery for impending myocardial infarction. *Circulation* 44: 11-102, 1971.
10. Hultgren, N. H.: Surgical versus medical management of unstable angina. *Amer J Cardiol* 38: 479-486, 1976.
11. Muller, D., Cannon, D., Fogarty, T.: Saphenous vein coronary artery bypass in patients with pre-infarction angina. *Circulation* 47: 234, 1973.
12. Bonchek, Rahimtoola, S., Anderson, R.: Late results following emergency saphenous vein bypass grafting for unstable angina. *Circulation* 50: 972, 1974.
13. Takaro, T., Hultgren, H., Detrex, V. A.: Cooperative study of coronary arterial surgery II. Left main disease (abstr). *Circulation* 52: Suppl II:11 - 143, 1975.
14. Gazes, P., Mobley, E., Faris, H.: Pre-infarctional (unstable) angina: a prospective study - ten year follow-up. *Circulation* 48: 331, 1973.
15. Fischl, S., Gorlin, R., Herman, M. V.: The intermediate coronary syndrome: Clinical, angiographic and therapeutic aspects. *N Engl J Med* 288: 1193-1198, 1973.
16. Pitt, B., Weiss, J. L., Schulze, R. A., Taylor, D. R., Kennedy, H. L., Caralis, D.: Reduction of myocardial infarct extension in man by propranolol (abstr). *Circulation* 54, 4: 109, 1976.
17. Chatterjee, K., Swan, H. J. C., Parmely, W. W., Sustaita, H., Marcus, H., Matloff, J.: Depression of left ventricular function due to acute myocardial ischemia and its reversal after aorto coronary saphenous vein bypass: *N Engl J Med* 286: 1117, 1972.




**B.W. CO. MAKES CODEINE ANALGESICS.  
YOU MAKE THE CHOICE.**



# **EMPIRIN<sup>®</sup>**

## **COMPOUND c CODEINE #3**

Each tablet contains: codeine phosphate, 32 mg (gr ½), (Warning: May be habit-forming); aspirin, 227 mg; phenacetin, 162 mg; and caffeine, 32 mg. 

### **The classic codeine pain reliever**

For decades, Empirin Compound c Codeine #3 has provided potent analgesia plus the anti-inflammatory action of aspirin for consistently dependable pain relief in the majority of your pain patients. Brand name quality at reasonable cost; readily available in hospital and local pharmacies.

Plus CIII prescribing convenience: up to 5 refills in 6 months (where state law permits), and telephone prescribing permissible in most states. See page 3 of advertisement for prescribing information.

**NOW...**



# COLBY PROCLAIMS WOMAN SUFFRAGE

Signs Certificate of Ratification  
at His Home Without  
Women Witnesses.

MILITANTS VEXED AT PRIVACY.

Wanted Movies of Ceremony,  
But Both Factions Are

WASHINGTON, Aug. 26, 1920—  
struggle for wom-



## TRUMAN CLOSES UNITED NATIONS CONFERENCE WITH PLEA TO TRANSLATE CHARTER INTO DEEDS

### NEW WORLD HOPE

President Hails 'Great  
Instrument of Peace,'  
Insists It Be Used

HISTORIC LANDMARK

Meeting Gives Standing  
Ovation as Executive  
Pictures Peace Gain

"If we fail to use it," he declared  
to the solemn final meeting of the  
delegates, 'we shall betray all of  
those who have died in order that  
we might meet here in freedom and  
safety to create it.'

"If we seek to use it selfishly—for  
the advantage of any one nation or  
any small group of nations—we  
shall be equally guilty of that be-  
trayal."

Fervent Interpolation

The President, speaking in the  
auditorium of the War Memorial  
Opera House, built in memory of  
sons of the Golden Gate city who  
gave their lives in the first World  
War, in which he himself served,  
seemed to give unconscious expres-  
sion to the solemn feeling of the  
occasion when, at the outset of his  
speech, he interpolated the words,  
half a hope, half a prayer:

"Oh, what a great day this can  
be in history!"

# Social Security Bill Is Signed; Gives Pensions to Aged, Jobless

Roosevelt Approves Message Intended to Benefit 30,000,000  
Persons When States Adopt Cooperating Laws—He Calls  
the Measure 'Cornerstone' of His Economic Program

## SENATE APPROVES 18-YEAR OLD VOTE IN ALL ELECTIONS

Amendment to Constitution  
is Sent to House, Where  
Passage is Expected

WASHINGTON, March 10,  
1971—The Senate approved  
today 94 to 0 and sent to

WASHINGTON, Aug. 14,  
The Social Security Bill, pro-  
a broad program of unemplo-  
insurance and old age pen-  
and counted upon to benefit  
20,000,000 persons, became law  
day when it was signed by Pres-  
dent Roosevelt in the presence of  
those chiefly responsible for  
financing it through Congress.

Mr. Roosevelt called the bill  
"the cornerstone of my economic  
policy which is being put into  
effect by the Social Security Act."  
The bill is a complete  
reform of the old-age pension  
system.

## the Draft Ends No

WASHINGTON, Jan. 27,  
1973—"With the signing of  
the peace agreement in  
Paris today, and after re-  
ceiving a report from the



---

# PATIENT PACKAGE INSERTS: A CONCEPT WHOSE TIME HAS COME?

---

*The consumer's right to know is an irreversible and desirable trend of the Seventies. It extends, and properly, to a patient's right to know more about his or her prescription medications. One way, gaining favor, is through patient package inserts. Wisely-prepared and properly distributed when medically indicated, they could markedly improve patient knowledge and drug therapy—laudable goals by anyone's standards.*

*The PMA endorses these goals and will work with government, the health professions and consumers to achieve them.*

## **The Advantages**

The concept holds promise of benefits: better patient understanding of the product prescribed, better adherence to the treatment plan, and more awareness of possible side reactions.

Every doctor has had patients who fail to finish antibiotic regimens because they feel better. Some patients assume that if one tranquilizer or analgesic is good, two may be twice as good. Still others fail to report dizziness while on antihypertensive therapy—and so on.

Problems like these might arise less often if the patient received written information in addition to verbal instructions. Some studies suggest that patients are more receptive to such materials, and they more often understand the verbal instructions and follow them, when inserts are used.

## **The Disadvantages**

There are also some potential problems. Obviously, the inserts must be clearly phrased, without extraneous or complex detail. How much information

is enough? How can it be kept current? Should all patients receive the same information? Should inserts be included with all drugs? Should only potential problems be listed or are patients better off with a "fair balance" presentation that describes usefulness as well as drawbacks?

These and similar questions require answers, since model inserts have yet to be properly developed and tested. Despite the need for these studies, the FDA is proceeding prematurely with inserts on selected products. We think the Congress is the only place where the matter can be given the proper legal status and direction, particularly since it represents a conceptual change in the legal, medical and social framework of the nation's prescription drug information system.

## **The Solution**

The PMA believes that carefully-devised pilot studies of various kinds of inserts are needed. They should be developed and implemented with full participation by doctors, pharmacists, consumers, communications experts and the drug industry. Such studies will provide reliable pathways to follow, so that inserts will be useful aids to medical practice.

And particularly we think that you should be closely involved in this debate and in these studies and decisions. Otherwise, people with less experience and qualifications may control the purposes, content and use of a tool with considerable promise for improved patient care. It could make a difference in your practice tomorrow, and more importantly, in the health of your patients.

**PMA**

THE PHARMACEUTICAL MANUFACTURERS ASSOCIATION  
1155 FIFTEENTH ST., N. W., WASHINGTON, D. C. 20005



Lidov



# When choosing a diuretic for day-in-day-out hypertension control with comfortable compliance...

The agent you choose in mild to moderate essential hypertension should offer (1) long-term effectiveness, (2) patient comfort and compliance.

**Zaroxolyn offers both.**

In one long-term study<sup>1</sup> Zaroxolyn brought moderately elevated (average 161/109 mm Hg) blood pressure down to the range of normotension—and held it there for a year or more.

The investigator noted, "Patient cooperation was surprisingly good for a study of such duration [2½ years]. The once-daily dosage schedule with

metolazone [Zaroxolyn] no doubt contributed to patient compliance."

Overall compliance with Zaroxolyn is good—very good. An analysis of controlled clinical studies involving 188 Zaroxolyn patients showed that only eight discontinued therapy because of side effects. That's a discontinuation rate of only 4.3%, and broader clinical experience appears to substantiate this low rate?<sup>2</sup>

Zaroxolyn. For long-term control and comfortable compliance in mild to moderate hypertension.

**Recommended initial dosage in mild to moderate essential hypertension—2½ to 5 mg once daily**

**Zaroxolyn®**  
(metolazone, Pennwalt)

2½-mg, 5-mg and 10-mg tablets

**once-daily antihypertensive diuretic**


Before prescribing, see complete prescribing information in the package insert, or in PDR, or available from your Pennwalt representative. The following is a brief summary. **Indications:** Zaroxolyn (metolazone) is an antihypertensive diuretic indicated for the management of mild to moderate essential hypertension as sole therapeutic agent and in the more severe forms of hypertension in conjunction with other antihypertensive agents. Also, edema associated with heart failure and renal disease. **Contraindications:** Anuria, hepatic coma or precoma, allergy or sensitivity to Zaroxolyn. Or, as a routine in otherwise healthy pregnant women. **Warnings:** In theory cross-allergy may occur in patients allergic to sulfonamide-derived drugs, thiazides or quinethazone. Hypokalemia may occur, and is a particular hazard in digitalized patients; dangerous or fatal arrhythmias may occur in hypokalemia and hyperuricemia may be noted or precipitated. Considerable potentiation may occur when given concurrently with furosemide when used concurrently with other antihypertensives, the dosage of the other agents should be reduced. Use with potassium-sparing diuretics may cause potassium retention and hyperkalemia. Administration to women of childbearing

age requires that potential benefits be weighed against possible hazards to the fetus. Zaroxolyn appears in the breast milk. Not for pediatric use. **Precautions:** Perform periodic examination of serum electrolytes, BUN, uric acid, and glucose. Observe patients for signs of fluid or electrolyte imbalance. These determinations are particularly important when there is excessive vomiting or diarrhea, or when parenteral fluids are administered. Patients treated with diuretics or corticosteroids are susceptible to potassium depletion. Caution should be observed when administering to patients with gout or hyperuricemia or those with severely impaired renal function. Hyperglycemia and glycosuria may occur in latent diabetes. Chloride deficit and hypochloremic alkalosis may occur. Orthostatic hypotension may occur. Dilutional hyponatremia may occur in edematous patients in hot weather. **Adverse Reactions:** Constipation, nausea, vomiting, anorexia, diarrhea, bloating, epigastric distress, intrahepatic cholestatic jaundice, hepatitis, syncope, dizziness, drowsiness, vertigo, headache, orthostatic hypotension, excessive volume depletion, hemoconcentration, venous thrombosis, palpitation, chest pain, leukopenia, urticaria, other skin rashes, dryness of mouth,

hypokalemia, hyponatremia, hypochloremia, hypochloremic alkalosis, hyperuricemia, hyperglycemia, glycosuria, raised BUN or creatinine, fatigue, muscle cramps or spasm, weakness, restlessness, chills, and acute gouty attacks. **Usual Initial Once-Daily Dosages:** mild to moderate essential hypertension—2½ to 5 mg; edema of cardiac failure—5 to 10 mg, edema of renal disease—5 to 20 mg. Dosage adjustment may be necessary during the course of therapy. **How Supplied:** Tablets, 2½, 5 and 10 mg

#### References:

- 1 Dornfeld L, Kane R. Metolazone in essential hypertension. The long-term clinical efficacy of a new diuretic. *Curr Ther Res* 18: 527-533, 1975
- 2 Data on file. Medical Department, Pennwalt Prescription Products

 **PENNWALT**  
Pennwalt Prescription Products  
Pharmaceutical Division  
Pennwalt Corporation  
Rochester New York 14603

# If the AMA didn't speak for the profession, who would?

Who would speak for the profession on the 2,500 health bills introduced in every Congress? Or the regulations issued by federal agencies?

Who would state the profession's views on national health insurance? Utilization Review Regulations? The Health Planning Act of 1974? Maximum Allowable Cost Regulations? Health Manpower?

Who would provide the scientific input and the practitioner's experience and knowledge so essential to legislation on drugs, cancer, heart disease, communicable diseases? Can you think of anyone?

The fact is, there is only one organization that can — and does — speak for the profession as a whole. The AMA.

It does so to protect the basic freedoms of medical practice in any federal health program that might be enacted; and even more important, to promote legislation for better health care for the entire public.

The AMA's voice can only be as strong as the members of the profession choose to make it. With your support, the AMA can be even more effective spokesman.



**Join us.**  
**We can do much more together.**

Dept. of Membership Development  
American Medical Association  
535 N. Dearborn St./Chicago, IL 60610

Please send me more information on the AMA  
and AMA membership.

Name \_\_\_\_\_

Address \_\_\_\_\_

City/State/Zip \_\_\_\_\_

# DANTROLENE SODIUM: AN EFFECTIVE THERAPEUTIC AGENT FOR THE TREATMENT OF SPASTICITY IN CHILDREN

José M. García-Castro, M. D.

**Summary:** We have studied the use of dantrolene sodium for the management of spasticity in 7 retarded and spastic children. In all of our cases improvement was observed with no untoward effects. The drug was used as a 1mg/ml suspension, the dosage being titrated for each patient. An average dose of 3.75 mg/kg/day with a range of 0.5 to 12.8 mg/kg/day was used in our patients. The results indicate dantrolene sodium to be an effective and probably safe drug for the management of spasticity in children.

**Resumen:** El uso de dantrolene sódico para el manejo de la espasticidad fue evaluado en 7 niños retardados y espásticos. En todos los casos se observó una mejoría franca, sin problemas secundarios o complicaciones. La droga se preparó como una suspensión con concentración de 1 mg/ml y la posología a usarse se determinó individualmente en cada paciente. La dosis promedio fue de 3.75 mg/kg/día, con una dispersión de 0.5 a 12.8 mg/kg/día. Los resultados

indican que el dantrolene sódico es una droga efectiva y probablemente segura para el manejo de la espasticidad en los niños.

The medical management of retarded children, particularly when the condition is also associated with spasticity, can be fraught with anxiety, both from the physicians' and the parents' standpoints, for the therapeutic modes available are often quite limited and the outcomes, unfortunately, are most of the times not up to expectations.

As a result of our work in the Regional Medical Program Project for Hereditary Diseases, we have been exposed to many cases of severely retarded, spastic children. In many we have been able to ascertain the fact that parental anxiety has not been so much the result of the retardation present, for many had already come to grips with the diagnosis and its implications, but because of the spasticity, which often prevented the parents from performing adequately the basic care of their children, such as feeding, toilette, etc. The latter, particularly, can evoke tremendous anxiety, for when faced with the impossibility of improving their children's mental status, most parents in our milieu derive great satisfaction of at least being able to maintain their affected children well-groomed and clothed. A release from the difficulties of performing these tasks was what many parents demanded of us. This steered us into a search for therapeutic means to relieve the spasticity enough so as to render these tasks feasible.

---

*From the Regional Medical Program for Hereditary Diseases and the Medical Genetics Section, Department of Pediatrics, University Children's Hospital, School of Medicine, Medical Sciences Campus, University of Puerto Rico, San Juan, Puerto Rico.*

*Supported in part by Grant 1G04-RM-0000-CA-01 of the Regional Medical Program, National Institutes of Health, Bethesda, Maryland.*

*Reprint address: Dr. José M. García-Castro, Programa Médico Regional de Enfermedades Hereditarias, G. P. O. Apartado 1764, San Juan, Puerto Rico 00936.*



In 1964, dantrolene sodium, a muscle relaxant exerting its effect peripherally upon the muscle directly and with virtually no central nervous system effects was introduced. However, clinical trials with the drug were not reported until 1973 (1, 2) and its use in children even later (3). In the latter, the efficacy of dantrolene sodium was studied in 23 retarded, spastic children, the results showing improvement in all cases with no untoward effects. This moved us to a trial of this drug, as these results have not been reconfirmed. For almost a year now we have carried out a pilot study on the effects of dantrolene sodium on a selected group of retarded and spastic children followed in our clinic. Our observations to date form the basis for this report.

### Methods

Since dantrolene sodium has been used mainly on adults, pediatric preparations are not available. The drug (Dantrium®) is regularly obtained in 25 or 100 mg capsules. To overcome this problem, we proceeded to make a suspension of the contents of a 100 mg capsule in 100 ml of water (1 mg/ml) and began titrating the dosage needed to obtain the desired effects, that is, the improvement or the disappearance of the spasticity.

For this report, we wish to present our experience on seven retarded, spastic children with ages ranging from 2 to 8 years. At present we have placed more children on this regime, but the time of evaluation has been short, thus we have not included them in this series. Before placement on the therapeutic trial, the patients were evaluated clinically, particularly to ascertain the extent and severity of the spasticity. The method used included evaluation of the range of motion, active and passive, of all of the articulations, including neck, the extremities and digits, and pelvis. The presence or absence of ankle clonus was also noted. The parents were instructed also in the assessment of these functions. They were encouraged to observe any changes in the difficulties encountered in the daily, routine management of the children. Baseline laboratory studies were performed, which included a complete blood count, urinalysis and SMA-12, and were repeated periodically. The dosage of the drug administered initially was 1 mg bid and a re-evaluation of the patients was effected

every 1-2 weeks. The dosage was incremented gradually, until the desired response was observed and no further changes could be elicited. The patients were maintained then at this dosage and seen at monthly intervals.

### Results and Discussion

The use of dantrolene sodium as described proved to be every effective for obtaining an improvement of the spasticity in all of the patients studied. Active and passive range of motion increased for all of the articulations tested. Even in those with ankylosis, improvement was observed, albeit to a lesser degree, which indicates the need to commence treatment early, before ankylosis sets in. Clonus, when present, also disappeared with treatment. This improvement was ascertained through our periodic clinical examinations, as well as through the parents' and physical therapists' evaluations, the latter being unaware that the child was receiving a muscle relaxant at the time. Moreover we have observed in one of the children, that after a brief (one month) course of dantrolene sodium at a dosage of 0.5 mg/kg/day, the spasticity disappeared and has not recurred, in spite of having been completely off therapy for over two months. Thus it may be that cessation of therapy after the child has overcome the problem of the spasticity may not cause a re-appearance of the symptoms. This we are studying at present.

As may be expected, the dosage required to produce the desired effects varied with each child, the result of individual pharmacological kinetics known to occur with this drug (4). The average maintenance used was 3.75 mg/kg/day, with a range of 0.5 to 12.8 mg/kg/day. At none of these dosages were any untoward effects observed. Neither have we found abnormalities in any of the laboratory tests performed. We have already observed a patient for 15 months on the highest maintenance dose (12.8 mg/kg/day), without the appearance of complications, which suggests the safety of the drug at relatively high dosages and prolonged time of

usage.

An unexpected result has been the observation that the effects of the drug were not limited to the improvement of the spasticity of the extremities and the vertebral column, which is what is usually assessed, but also upon functions such as deglutition, articulation of sounds, control of eye movements, smiling, etc., with the result that the children have not only improved in appearance and gained weight, but have also become more aware of their surroundings. This has permitted most of them to respond emotionally to their parents' caresses, a fringe-benefit of the therapy which neither the parents nor ourselves thought possible a priori.

In conclusion, our study demonstrates that dantrolene sodium appears to be an effective drug in the management of spasticity in children and seems to be safe even after prolonged usage. We strongly recommend individualization of the dosage used so as to maximize the improvement and minimize the risks of complications, which thus far we have not witnessed. Our mode of administration is not only practical, but also economical. Once in suspension, the drug keeps adequately under refrigeration for several weeks.

Dantrolene sodium seems to be, thus, a breakthrough in the treatment of spasticity.

### Reconocimiento

Queremos agradecer las sugerencias del Dr. Jesús Vélez-Borrás, quien nos encaminó en este proyecto, como el trabajo de la Sra. Edna G. de Arenado del Programa Médico Regional de Enfermedades Hereditarias, y de todos los padres de los niños que participaron en el estudio, los verdaderos ejecutores del mismo.

### Referencias

1. Mayer, N., Mecomber, S. A. and Herman, R.: Treatment of spasticity with dantrolene sodium. *Am. J. Phys. Med.* 52 (1): 18-29, 1973.
2. Chyatte, S. B. and Basmajian, J. V.: Dantrolene sodium: Long-term effects in severe spasticity. *Arch. Phys. Med. Rehabil.* 54: 311-315, 1973.
3. Haslam, R. H. A., Walcher, R., Lietman, P. S., Kallman, C. H. and Mellits, E. D.: Dantrolene sodium in children with spasticity. *Arch. Phys. Med. Rehabil.* 55: 384-388, 1974.
4. Lietman, P. S., Haslam, R. H. A. and Walcher, R.: Pharmacology of dantrolene sodium in children. *Arch. Phys. Med. Rehabil.* 55: 388-392, 1974.

## MYCOTIC PULMONARY ARTERY ANEURYSMS: A RARE CAUSE OF FATAL HEMOPTYSIS

Hernán D. Giraldo, MD and José Ramírez Rivera, MD

**Summary:** A case of unrecognized infectious endarteritis producing multiple pulmonary aneurysms and recurrent and ultimately fatal hemoptysis is presented. Gradual development of aneurysms and arterial thromboses was documented by angiograms and a scintigram. Twenty-five blood cultures obtained over a period of five months showed no growth. The limited blood flow through mycotic aneurysms explains why blood cultures are frequently negative in this disease. It may be hard to distinguish mycotic aneurysms from inflammatory or neoplastic lesions. Persistent leukocytosis, recurrent fever and the development of persistent shadows with changing contours may suggest the correct diagnosis.

**Resumen:** Se presenta un caso de endarteritis infecciosa de la arteria pulmonar. Esta no fue reconocida por nueve meses. Produjo múltiples aneurismas pulmonares y recurrentes hemoptisis una de las cuales finalmente causó la muerte del paciente. El desarrollo gradual de las aneurismas y las trombosis arteriales fue documentada por angiogramas y escintigramas. Veinticinco cultivos de sangre obtenidos durante un período de cinco meses fueron negativos. El flujo limitado de sangre a través de una aneurisma micótica explica porque los cultivos de sangre son frecuentemente negativos en esta enfermedad. Puede ser difícil diferenciar aneurismas micóti-

cas del pulmón de lesiones inflamatorias o neoplásicas. Una leucocitosis continua, fiebre recurrente e imágenes radiográficas de bordes cambiantes pueden sugerir el diagnóstico correcto.

Pulmonary arteriovenous aneurysms are not rare but their clinical presentation is frequently misinterpreted. Their signs and symptoms are confused with inflammatory or neoplastic parenchymal lesions.

Although most aneurysms are manifestations of the uncommon disease hereditary hemorrhagic telangiectasia (2), others are acquired and are commonly caused by infection.

Many mycotic causes of pulmonary aneurysms have been reported: Schistosomiasis (3), Syphilis (4), Tuberculosis (5), persistent ductus arteriosus with endarteritis, mitral and aortic endocarditis (12), lung abscess (4-6), recurrent thromboembolism (11-12), tricuspid endocarditis (13), and teeth extraction (14). "Mycotic-like" pulmonary aneurysms have been observed in association with trauma (15) and polyarteritis nodosa (16). The cause of others defies identification (17).

We report here the tragic case of an unrecognized pulmonary infectious endarteritis in a young man without heart disease or a specific source for infected emboli. The endarteritis caused multiple pulmonary aneurysms, hemoptysis and finally fatal hemorrhage.

### Case Report

A 14-year old white boy was admitted for the

---

*From the Department of Medicine, Mayagüez Medical Center, Puerto Rico.*



second time to the Mayagüez Medical Center (MMC) on December 15, 1975 with intermittent hectic fever, chills, hemoptysis and weight loss.

He was in good health until April 1975 when repeated episodes of chills and fever developed. Two months later, in June, he sought attention at the MMC with persistent fever and chest pain. At that time a hematocrit of 38 percent and a white-cell count of 18,400 per cu mm was noted. A 3 x 2cm round shadow was noted just below the left hilum. The urinary sediment showed 2-4 red blood cells per high power field. Five hundred milligrams of oral ampicillin were administered three times daily and he was asked to return 8 days later, but he failed to keep his appointment.

On August 11, 1975 he was hospitalized for the first time with an intermittent hectic fever. He had been continuously febrile since first seen, but in the preceding month, daily fever spikes and shaking chills at the rate of 4-5 times a week had appeared and blood tinged sputum and dyspnea on exertion had developed. He had lost 12 pounds in the preceding four months; his weight had been reduced to a meager 65 pounds.

The boy denied testicular pain. There was no familiar history of tuberculosis, hemoptysis, gross hematuria, gastrointestinal bleeding, coagulation problems, epistaxis, cerebrovascular accidents or telangiectasia.

During his admission in August an ejection murmur grade 2/6 was heard at the second left intercostal space; no murmurs or rales were audible over the lung fields.

No cause for the septic fever was found; a transtracheal aspirate showed no bacteria and was sterile on culture, seven blood cultures were negative. The roentgenogram of the chest showed persistence of the 3 x 2cm round shadow previously seen just below the left hilum. At bronchoscopy blood was seen to ooze from the left lower lobe but no bleeding site could be identified. The hemoptysis continued and the intermittent hectic fever and leukocytosis persisted. From August 13 to August 21, 1,500 ml of whole blood were required to maintain the hematocrit at the level noted on admission, 25 percent. On August 25 he was transferred to the University Hospital for pulmonary surgery. Hemoptysis continued there and eleven additional blood cultures were negative.

On September 11 a left lower lobectomy was performed. The specimen showed a round cavity 10cm

in diameter containing clotted blood and fibrin. The resected specimen was interpreted pathologically as a bleeding bronchial cyst.

An arteriogram after surgery showed no abnormalities of the right pulmonary vascular tree. The 2 x 3cm density noted in the plain film near the left hilum was identified as being of vascular origin. There was no further hemoptysis after surgery but the chills and fever persisted, although he received therapy with clindamycin, gentamicin and ampicillin. The patient was discharged on ampicillin 500mg every 8 hours and failed once more to appear to his scheduled follow up visits.

On November 3, six weeks after his discharge, he returned to the emergency room at Mayagüez; intermittent fever and chills, at least five times a week, had continued; the white-cell count was 13,700 per cu mm. The hemoptysis had not recurred since his operation two months previously. In his chest roentgenogram, a small irregular infiltrate was seen at the anterior segment of the right upper lobe next to the minor fissure.

He was discharged on ampicillin 500 mg every eight hours. Ten days later, on November 13, he returned again to the emergency room. Hectic fever, and chills had persisted and now the sputum was again blood-streaked. Treatment was once more initiated with ampicillin without effect. On December 15, he sought admission to the MMC for the last time.

His height was 156 cm and his weight was 27.2 Kg; he was emaciated and pale. The temperature was 39° C. and white blood cell count 17,900 per cu mm. There was no clubbing of the fingers; and no telangiectasia or petechiae were found on careful examination of the skin, conjunctiva, ocular fundi, lips or mucosal surfaces. The left thoracotomy scar had healed well. There was dullness at the left base. Breath sounds were decreased at that base and both apices. No cardiac or pulmonary murmurs were heard. The testes were of normal size and were not tender.

During his hospitalization he had frequent chills, an intermittent hectic fever and persistent leukocytosis.

Seven additional blood cultures were negative. An intravenous pyelogram showed no abnormalities. The initial arterial oxygen and carbon dioxide tensions were 81 and 30mm Hg respectively; after administering 100 percent oxygen by mask, the oxygen tension increased only to 329 mm Hg. In the absence of obstructive airway disease this suggested an arteriovenous shunt. Prominent S waves in  $L_1$ , and  $L_2$  and inverted T waves in  $V_2$ - $V_4$  in the electrocardiogram were inter-

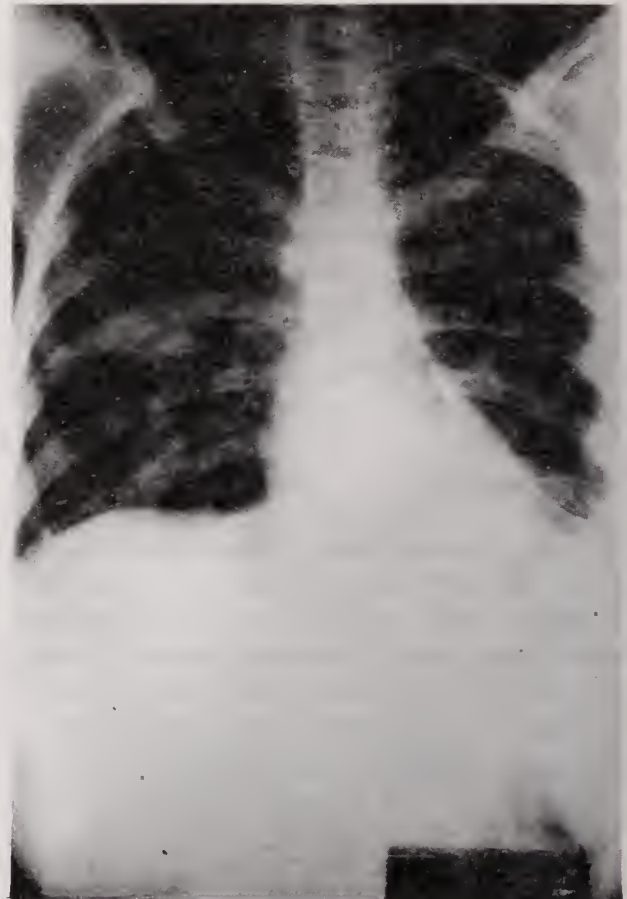


Figure 1: Chest radiographs 24 h apart. (A) dated December 17 showing an extensive pneumonic infiltrate in the anterior segment of the right upper lobe and in the right lower lung field. A nodular density near the left hilum has reappeared; (B) dated December 18 showing rapid resolution of the radiodensities.



Figure 2: Pulmonary scintigram dated December 12, 1975. Posterior view showing multiple perfusion defects at the periphery and apices of both lungs.

interpreted as right ventricular overload. The serum electrophoresis showed an increase of all globulin fractions and a low albumin. Sudden chest infiltrates that rapidly disappeared were observed in association with persistent hemoptysis (Fig. 1). Multiple perfusion defects appeared in the scintigram at both apices and the right base (Fig. 2). A pulmonary angiogram showed 4 aneurysmal dilatations of the pulmonary artery in the right lung and 2 on the left lung; perfusion was diminished at the apices (Figs. 3A and 3B). The pulmonary veins filled precociously.

On December 30, considering for the first time the possibility of a bacterial pulmonary arteritis, therapy with 20 million units of aqueous penicillin and 120 mg units of garamicin daily was initiated. The patient's appetite improved after 4 days of therapy and chills stopped on the 5th day. The white blood cell count diminished from 20,000 to 14,000. On January 3, he developed a stabbing pain. A right pleural rub was best heard at





Figure 3: Selected postero-anterior views of pulmonary angiogram on December 30, 1975. (A) arterial phase showing three rounded vascular shadows in the right lung and one in the left. There are perfusion defects in apices and bases; (B) venous phase showing persistence of contrast media in the aneurysmatic lesions previously visualized.

7th and 8th intercostal spaces. The rub persisted until his sudden death on January 8 of massive pulmonary hemorrhage, eight days after initiating the administration of antimicrobials.

Autopsy revealed 4 pulmonary artery aneurysms in the right lung and one in the left with diameters ranging from 2 to 5 cms. Multiple arterial thrombi were present in the apices and in the periphery of both lungs. Microscopic examination showed an intimal endarteritis with polymorphonuclear infiltration with complete destruction of the media in several areas. There were bacteria trapped in thrombi in some of the arterial lumina. The liver weighed 1,800 gm and showed chronic passive congestion. Kidneys and testes were normal in weight and appearance and histologically

showed no abnormalities. No granulomatous lesions nor eosinophilic infiltrations were seen.

### Discussion

The term "mycotic" aneurysms is attributed to William Osler (18). The term implies a bacterial invasion of the media of an arterial wall by blood-born microorganisms or organisms from an adjacent parenchymal inflammation.

Although no source of septic emboli was found, the clinical course and the sequential angiograms in this case suggest that the fundamen-



tal pathologic process was a blood-born infectious arteritis. Aneurysms developed gradually and in multiple sites as a consequence of the persistent arterial infection. Recurrent hemoptysis occurred, and eventually the patient died of pulmonary hemorrhage. The persistent pulmonary arterial infection remained unrecognized for nine months.

The primary pathologic process explains in part the lack of the characteristic manifestations generally seen in patients with congenital arteriovenous aneurysms: cyanosis, polycythemia and finger-clubbing. These manifestations were absent because extensive pulmonary arterial thrombi limited the functional aspects of the impressive arteriovenous communications seen angiographically and confirmed at autopsy.

A pulmonary arteritis bears little resemblance to an endocarditis or an arteritis of the systemic circulation where streams of blood under high pressure constantly bathe rigid valves or vessels, where infectious organisms keep their foot-hold with great difficulty. The modest blood flow through these aneurysms in a compliant low pressure system of multiple collateral channels amply explains the puzzling aspect of negative blood cultures in cases of mycotic pulmonary aneurysms.

It may be hard to distinguish mycotic aneurysms from inflammatory or neoplastic lesions. Persistent leukocytosis, recurrent fever and the development of persistent shadows with changing contours may suggest the correct diagnosis. Only pulmonary angiography can provide the definitive answer by separating vascular from nonvascular pulmonary lesions. Characteristically the aneurysms opacify when the pulmonary artery is filled and remain filled during the venous phase.

The sudden appearance of rounded masses in association with hemoptysis and fever raised the possibility that this patient had polyarteritis. However, at autopsy no other organs showed recent or old manifestations of arteritis and the histologic sections did not bear out this suspi-

cion.

Thromboembolic phenomena as well as arterial perforation have been observed as complications of indwelling pulmonary arterial catheters (19-20). Although no mycotic aneurysms have been reported as complications of indwelling catheters, one should be aware that these might occur.

## References

1. Deterling, R. A., Jr., Clagett, O. T.: "Aneurysms of the pulmonary artery". Review of the literature and report of a case. *Am Heart J*: 34, 471-499, 1947.
2. Hodgson, C. H., Burchell, H. B., Good, C. A., et al: "Hereditary hemorrhagic telangiectasia and pulmonary arteriovenous fistulas". *N Eng J Med*: 261, 625-636, 1959.
3. Jaffe, R. B., Condon, V. R.: "Mycotic aneurysms of the pulmonary artery and aorta". *Radiology*: 116, 291-298, 1975.
4. Calenoff, L.: "Multiple mycotic pulmonary artery aneurysms". *Am J Roentgenol*: 91, 379-384, 1964.
5. Kauffman, S., Lynfield, J., Hennigar, G.: "Mycotic aneurysms of the intrapulmonary arteries". *Circulation*: 35, 90-99, 1967.
6. Gorodezky, M., et al: "Mycotic aneurysms of the pulmonary artery". *Chest*: 66, 214-216, 1974.
7. Goh, T. H.: "Mycotic aneurysms of the pulmonary artery". *British Heart J*: 36, 387-390, 1974.
8. Pirani, C., Ewart, F., Wilson, Andrey: "Thromboendarteritis with multiple mycotic aneurysms of branches of the pulmonary artery". *Am J Dis of Children*: 77, 460-473, 1949.
9. Roberson, C. K. A.: "Arteriovenous aneurysms of the lung with pulmonary tuberculosis". *Brit J Tuberc*: 44, 58-61, 1950.
10. Warthin, A. S.: "Syphilis of the pulmonary artery". *Am J Syph*: 1, 693-711, 1917.
11. DeFaria, J. L., Barbas, V., Fujioka, T., et al: "Pulmonary schistosomatic arteriovenous fistulas producing a new cyanotic syndrome in manson's schistosomiasis". *Am Heart J*: 58, 556-557, 1959.
12. Jacobson, F. A., Foch, G., Liliequist, B.: "Multiple pulmonary artery aneurysms". *Acta Med Scand*: 179, 673-678, 1963.
13. Kidd, P.: "Embolic aneurysms of the pulmonary artery". *Trans Path Soc (London)*: 44, 47, 1893.
14. Palmer, H. D., Kempf, M.: "Streptococcus viridans bacteremia following extraction of teeth". Case of multiple mycotic aneurysms in the pulmonary arteries: *JAMA*: 113, 1788-1792, 1939.
15. Symbas, P. N., Scott, H. W., Jr.: "Traumatic aneurysms of the pulmonary artery". *J Thorac Cardiovasc Surg*: 45,

- 645-649, 1963.
16. *Eskelund, V.*: "Periarteritis nodosa der pulmonarterie und primäre pulmonalsklerose". *Acta Path et Microbiol Scand*: 19, 13-, 1943.
17. *Monchick, J., Wilkins, E.*: "Solitary aneurysms of the middle lobe artery". *Ann Thorac Surg*: 17, 496-503, 1974.
18. *Osler, W.*: "The gulstonian lecture on malignant endocarditis". *Br Med J*: 1, 467-470, 1885.
19. *Chun, G. M., Ellestad, M. H.*: "Perforation of pulmonary artery by a swan-ganz catheter". *New Eng J Med*: 284, 1041-1042, 1971.
20. *Goodman, D. J., et al*: "Thromboembolic complications of balloon tipped pulmonary artery catheter". *N Eng J Med*: 291, 777, 1974.

## POLYCYSTIC LIVER DISEASE: CASE REPORT

A. H. Sarmiento, MD, A. E. Lanaro, MD and D. Vázquez, MD

Polycystic liver disease is a relatively rare disease of easy diagnosis when its possibility is considered. The authors wish to comment on the rational use of known non-invasive complementary methods that help to make a reliable diagnosis of this entity.

### Case Report

A fifty year old hypertensive female who was doing well until 1968 when, in a routine physical examination, she was found to have an enlarged liver. No specific evaluation was done and, subsequently, she was seen by different physicians who prescribed vitamin pills. The patient continued complaining of epigastric fullness and occasional bouts of vomiting. In September 1972, she was admitted to the University District Hospital for evaluation of hepatomegaly. At that time she denied history of jaundice, alcoholism, diarrhea, melena or hematemesis. She did have a history of river bathing and schistosomiasis was suspected. The liver scan showed multiple areas of decreased uptake and a liver biopsy failed to show any pathologic lesion. The liver function tests were within normal limits and rectal biopsy did not demonstrate ova of *schistosoma*

*mansoni*. Except for an eosinophilia of 13 percent, all other laboratory values were normal. A chest x-ray was negative. She was followed at the out-patient clinic where she received treatment of methyldopa and chlorothiazide for high blood pressure of 19-years' duration.



---

From the Nuclear Medicine Division, Center for Energy and Environment Research, Caparra Heights Station, San Juan, Puerto Rico 00935.

This paper was prepared in connection with work under contract No. E-(40-1)-1833 with ERDA. The Commission retains a non-exclusive royalty-free license in and to any copyrights covering this paper, with the right to authorize others to reproduce all or any part of the copyrighted paper.

Figure 1: Liver scan done with  $^{99m}\text{Tc}$  sulfur colloid with a dual rectilinear scanner - anterior view. It shows multiple and wide cold areas specially one at the superior pole of the right lobe. The right lung base is pushed very high.



In August 1975, another liver scan was performed which showed marked hepatomegaly and the presence of multiple "cold areas" (Figures 1 and 2). The image was found to be similar to that of the study done in September 1972. A radioangiogram and blood pool studies were done with routine technics (Figures 3 and 4). These showed avascularity of the lesions, suggesting that they were cystic. A renal scan (Figure 5 A-B) and an intravenous pyelogram demonstrated polycystic kidneys and added further confirmation of the disease and clarified the etiologic factor of her arterial hypertension. At the present time she has continued to do relatively well, except for the sensation of fullness in the epigastrium and her high blood pressure, which has been under control with methyldopa and chlorothiazide.

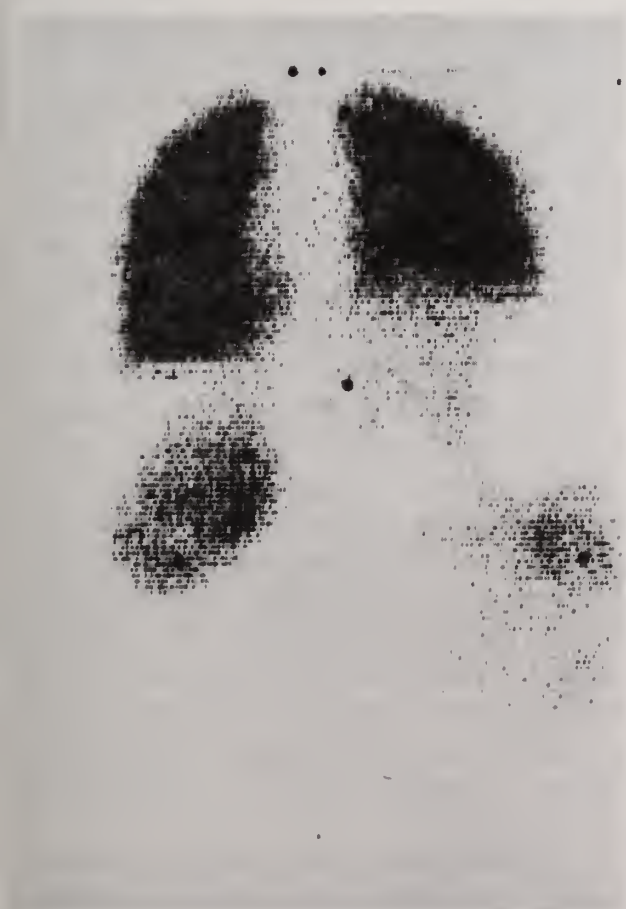


Figure 2: Same study - posterior view.

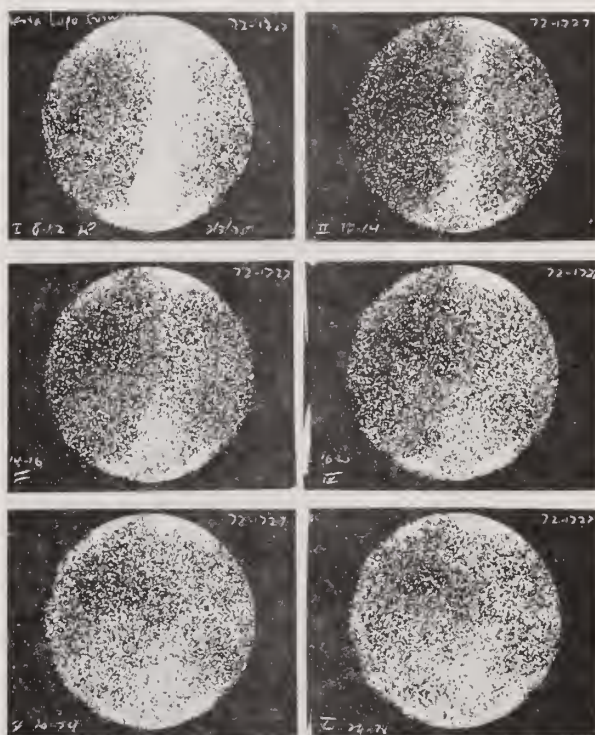


Figure 3: Liver radioangiogram with  $^{99m}\text{Tc}$  pertechnetate at the gamma camera. Sequential photos every 4 seconds. It shows avascularity of the cold areas.



Figure 4: Liver blood pool. After the radioangiogram the blood pool in a static image shows no blood in the pathologic areas.

TABLE I  
NON-INVASIVE METHODS THAT  
CONFIRM THE DIAGNOSIS OF POLYCYSTIC LIVER DISEASE

<i>Method</i>	<i>Findings</i>
<i>Liver Scan</i>	<i>Space occupying lesions (SOL) with or without hepatomegaly.</i>
<i>Liver Radioangiogram</i>	<i>Avascularity of SOL.</i>
<i>Liver Blood Pool Scan</i>	<i>Avascularity of SOL.</i>
<i>Kidney Scan and IVP</i>	<i>Show polycystic kidneys in about 50 percent of the cases.</i>
<i>Ultrasound</i>	<i>SOL with liquid pattern (echo free lesion)</i>

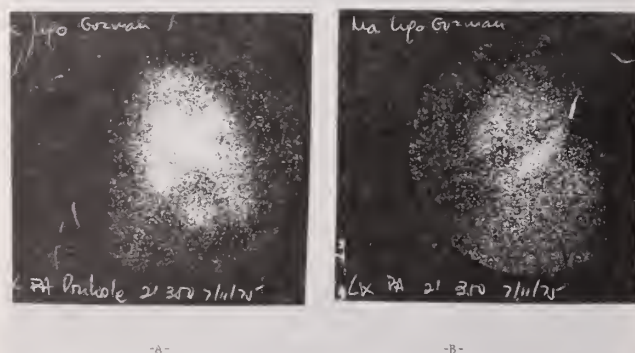


Figure 5: Renal scan with  $^{99m}\text{Tc}$  glucoheptonate shows big kidneys with multiple cold areas (polycystic kidneys).

### Discussion

Polycystic liver disease has a reported incidence of 0.53 percent in 1319 autopsies (1). Liver lesions are essentially degenerative and are abnormal extensions of the process of reabsorption which occurs normally in the first generation of bile ducts (2). Polycystic disease of the liver predominates in females between

the fourth and fifth decades but can be observed at all ages, including newborn and still-born (1). Cysts may be simple or multiple; from microscopic to 15 cm of diameter (3). The patient usually consults for symptoms referred to other associated pathology or, eventually, for complaints of weight or a mass in the upper right abdomen. Clinical examination reveals nodular hepatomegaly. This finding is not constant because the liver may be of normal size (6 cases of 24 with polycystic liver disease)(3). It must be remembered that a nodular hepatomegaly orients to a diagnosis but can be found in a liver within normal limits with one or several space-occupying lesions images in the scan. Laboratory and liver function tests are normal or very slightly abnormal (4). Polycystic liver disease is associated with polycystic kidneys in 51.6 percent of the cases. The inverse is not true and in polycystic kidneys a polycystic liver disease is associated in only 19 to 34.3 percent of the cases (1).

In the classical patient we find a relatively young, hypertensive woman with a mild hepatomegaly, normal laboratory values for liver function tests, and apparently healthy (5).

Complementary methods confirm the diagnosis (Table I).

Eventually, in a healthy patient without hepatomegaly or any other symptom, a space occupying lesion in the liver could be demonstrated by scanning.

If the focal lesions are well defined, the possibility of a false positive liver scan is remote. The pseudo-space-occupying lesions of cirrhotic liver may be ruled out by anamnesis, liver function tests and a suggestive liver scan. In this situation it is necessary to do a differential diagnosis of space occupying lesions by means of radioangiogram, blood pool scan and ultrasound. Usually, with these methods, it is possible to diagnose cystic lesions without celiac arteriography. Correct utilization of these auxiliary methods gives an early diagnosis with a minimum of discomfort and without trauma to the patient.

Polycystic liver disease is a benign entity

and its prognosis and treatment are given by the associated renal disease. A reliable and early diagnosis is important to give adequate treatment and avoid traumatic exploratory methods and unnecessary anxiety for the patient and physician.

### References

1. *Feldman, M.*: Polycystic disease of the liver. *The Am. J. of Gastroenterology* 29: 83-85, 1958.
2. *Norris, R. F., Tyson, R. M.*: The Pathogenesis of polycystic livers - Reconstructions of cystic elements on two cases. *Amer. J. Pathol.* 23: 201-209, 1947.
3. *Comfort, M. W., Gray, H. K., Dablin, D. C., Whitesell, F. B., Jr.*: Polycystic disease of the liver: A study of 24 cases. *Gastroenterology* 20: 60-78, 1952.
4. *Yarwood, C. R.*: Polycystic disease of the liver. *Brit. J. of Surgery* 45: 200-201, 1957.
5. *Gambill, E. E., Hodgson, J. R.*: Polycystic disease of the liver with unusual cholecystographic manifestations. Report of a case *Gastroenterology* 38: 1003-1004, 1960.



**BRIEF COMMUNICATION**  
**BLEEDING DUODENAL ULCER IN A PATIENT TAKING**  
**SLOW-RELEASING POTASSIUM TABLETS**

Pablo I. Altieri, MD, Carmelo Herrero, MD, Rómulo Suero, MD and Armando Ortíz, MD.

Some of the known complications of slow-releasing potassium tablets are:

1. Esophageal stricture
2. Esophageal ulceration
3. Small bowel ulceration and perforation (1-3)

That we know there has not been a report of a duodenal ulceration due to slow releasing potassium tablets. It is the purpose of this manuscript to report such a case.

**Case Report**

D. M. was a 69-year old female patient who is a known case of severe hypertensive cardiovascular disease, who was receiving guanethidine, furosemide, digoxin and liquid potassium chloride. The patient never complained of epigastric pain and never was treated for peptic ulcer disease. Upper gastrointestinal series done routinely a year ago was normal. During a follow up visit, we found that she was not taking the potassium chloride, because she disliked it. A slow-releasing potassium tablet (slow-K) was added to the therapy. She was started in one tablet three times a day. A week after the slow-releasing potassium tablets were given, she came

to the emergency room with massive rectal bleeding. Sigmoidoscopy and barium enema failed to show a bleeding lesion. Esophagoscopy were normal. Duodenoscopy showed the duodenum to be filled with bright red blood. She underwent exploratory laparotomy because she continued bleeding. During surgery, she was found with a normal duodenum, except a superficial ulcer which was actively bleeding. The ulcer was sutured and pyloroplasty with vagotomy was done.

The patient had a normal post operative period and she was discharged home on antihypertensive medication.

**Comments**

The purpose of this is to describe what we think is the first case of a bleeding duodenal ulcer due to a slow-releasing potassium tablet preparation. Usually the ulcers produced by these products are localized in the ileum or jejunum (1-3).

**References**

1. Howie, A. D., Strachan, R. W.: Slow release Potassium Chloride treatment. *Brit Med J.* 2: 176, 1976.
2. McCall, A. J.: Slow K Ulceration of esophagus with aneurysmal left atrium. *Brit Med J.* 3: 330, 1975.
3. Treasure, T.: Ulceration of small intestine and slow-releasing potassium tablets. *Brit Med J.* 3: 302, 1975.

---

*From the Font Martelo Hospital, Humacao, Puerto Rico.*

*SECOND PEDIATRIC NEPHROLOGY SYMPOSIUM:*

Will be sponsored by Georgetown University and the San Juan City Hospital, Condado Beach Hotel, San Juan, Puerto Rico, December 6 to 9, 1977. Topics include: Nephrologic Problems of the Newborn, Evaluation of the Patient with Renal Disease, Treatment of Renal Disease, Systemic Disease and the Kidney, Renal Physiology, Dialysis and Transplantation. Speakers are internationally known in the field of Nephrology. Accreditation in Category I for the Physician's Recognition Award has been applied for. Tuition: \$150 for physicians in practice; \$75 physicians in training with letter from chief of service.

For information write: José F. Pascual, MD, P. O. Box 3342, Old San Juan, Puerto Rico 00904.

---

*ANNOUNCING THE FOURTEENTH CONGRESS OF THE PAN-PACIFIC SURGICAL ASSOCIATION APRIL 1 - 7, 1978.*

Place: Hilton Hawaiian Village Hotel, Honolulu, Hawaii. Meeting Schedule: April 3 - 7, 1978 - concurrent meetings will be held in General Surgery, Neurosurgery, Obstetrics & Gynecology, Ophthalmology, Orthopaedic Surgery, Otolaryngology, Plastic Surgery, Thoracic-Cardiovascular, Urology.

April 3 - 5, 1978  
Colo-Rectal Surgery

April 6 - 7, 1978  
Anesthesiology

For details write to: Cesar B. de Jesús, MD, Pan-Pacific Surgical Association, 236 Alexander Young Building, 1077 Bishop Street, Honolulu, Hawaii 96813.

*FROM THE NETWORK FOR CONTINUING MEDICAL EDUCATION - 15 Columbus Circle New York City 10023:*

Below is a list of upcoming programs to be distributed by the Network for Continuing Medical Education. Please note that several of these programs are acceptable for the highest levels of formal continuing medical education credit by the AMA and AAFP.:

August 8 - September 4

**"CHRONIC HEMODIALYSIS: MAXIMIZING THE POTENTIALS,"**

with Eli A. Friedman, MD., Professor of Medicine, and Director of the Division of Renal Diseases, Downstate Medical Center, Brooklyn, New York.

**"ASSESSING THE CHILD WITH ACUTE ABDOMINAL PAIN,"**

with Russell S. Asnes, M.D., Director, Pediatric Ambulatory Services, and Associate Professor of Clinical Pediatrics, Columbia Presbyterian Medical Center, New York City.

**"THE UNDERGROWN INFANT: AN AMERICAN PROBLEM,"**

with Myron Winick, M.D., Director of the Institute for Human Nutrition, the R.R. Williams Professor of Nutrition, and Professor of Pediatrics, Columbia University College of Physicians and Surgeons, New York City.

September 5 - October 2

**"CLINICAL IMMUNOLOGY UPDATE"**

- \* The Mechanisms of Immune Competence
- \* Immune Deficiency Disorders
- \* Autoimmune Diseases

The telccourse faculty on this three part program

is Robert M. Nakamura, MD., Chairman, Department of Pathology, Scripps Clinic Medical Institutions, La Jolla, California and Ernest S. Tucker, MD., Associate Clinical Professor of Pathology and Pediatrics, University of California School of Medicine, San Diego.

### *DANGER AHEAD: RATIONING OF CARE*

In medicine as in other purchases, the buyer gets what he pays for. There is no steak-house medicine at hash-house prices. Prices of care cannot be harshly cut without cutbacks in the quality or quantity of care.

Those hard-boiled truths are obvious to us physicians, who deal with costs as a day-to-day reality rather than a pliable abstraction. And in its somewhat devious way, the federal government seems to perceive those truths, too.

The government's cluster of programs and proposals for containing costs is made to look like pure benefit for the patient, without any actual loss on his part. What they generally boil down to upon analysis, however, is rationing of care.

This was a central point —and a central danger— posed by Richard E. Palmer, MD., in addressing the AMA's annual convention last June as its outgoing president. Doctor Palmer identified rationing of care as a common denominator of proposed restraints in so-called unnecessary surgery covered by public funds, HMOs, the Health Planning Act of 1974, the push for generic drugs, and the proposed "cap" on hospital charges as a prelude to the Administration's National Health Insurance proposal.

On the proposed ceiling on hospital charges, he asked: "Is it not predictable that the most creative, resourceful, and conscientious hospitals would suffer from such economic artifice? Or that in treating all hospitals alike, the cap would penalize those that are already efficient, as a Senate health expert was quoted?"

Apropos hospitals, it also must be recognized that some lack efficiency; that some communities are over-bedded; and that costs —the Number One health-care concern of the public — can be restrained

without disastrous results to quality. The medical field—through such means as the AMA's Commission on the Cost of Medical Care — must do its practical best against the economics that encourage federal rationing of health services.

In the matter of HMOs, Doctor Palmer noted that these have been hailed on Capitol Hill as "a great piece of ammunition" against rising medical costs. But what about the amount of care? he wondered. Recent studies indicate that HMO physicians see their patients less often and give less service —including preventive care— than do fee-for-service physicians.

Shrinkage of service also could be the upshot of any NHI program that would ape Britain's National Health Service, said Doctor Palmer. For it has happened there.

As he summed up: "No individual—and ours is a nation of individuals— wants his care to fall victim to cost-effective common denominators. No individual wants his own care to be rationed."

Physicians at the local level should get this point across— as the government sharpens its ax against necessary costs.

### *PEDIATRIC DERMATOLOGY SEMINAR — MIAMI BEACH, FEBRUARY 23-26, 1978*

POST CONVENTION FLIGHT-CRUISE TO SOUTH AMERICA AND THE CARIBBEAN FEBRUARY 26 - MARCH 5, 1978

A three day Pediatric Dermatology Seminar will begin Thursday evening, February 23, 1978 at the Konover Hotel on the ocean front of Miami Beach, Florida. The program will conclude on Sunday afternoon, February 26, to be followed by a one week Post Seminar flight and cruise to the Caribbean and South America. Dr. R. Winkelmann, of the Mayo Clinic, will conduct daily lectures and discussions at Curacao, Caracas, Grenada, Guadeloupe, St. Thomas and San Juan.

The course is designed to review the most recent advances about skin diseases of children.

The tuition is \$150.00 for physicians and \$100.00



for physicians in training. For further details write to Guinter Kahn, MD, 16800 NW 2 Ave., Suite 401, North Miami Beach, Florida, 33169.

---

*V CONGRESO LATINOAMERICANO DE PEDIATRIA*  
*XII CONGRESO PANAMERICANO DE PEDIATRIA -*  
*XVI CONGRESO NACIONAL DE PEDIATRIA -*  
*24 AL 30 DE SEPTIEMBRE DE 1978 - PUERTO DE*  
*ACAPULCO, MEXICO.*

---

#### *PHYSICIAN LISTS SIGNS OF BUDDING ALCOHOLISM*

CHICAGO - The average alcoholic has been in difficulty with alcohol for ten years before he seeks help because of severe illness. If alcoholism is identified early, much destruction can be prevented. But it is exceedingly difficult to identify the early alcoholic.

The July 11 Journal of the American Medical Association offers for physicians some signs that may help them to identify early alcoholism in their patients.

The budding alcoholic hides the disease from his physician and, often, from himself. The doctor is advised to watch for certain symptoms often found in alcoholics. Heartburn is the most common. The alcohol abuser is frequently a user of over-the-counter antacids. Other symptoms may be morning cough, increased pulse rate, high blood pressure, tremors in middle age, bruises that might have been caused by stumbling, anxiety, tension and stress, insomnia, high blood sugar, and enlarged liver.

C. Nelson Davis, MD, of Malvern Institute, Malvern, Pa., suggests that the patient will understate the amount he drinks, but often is willing to discuss drinking habits. The doctor may learn about alcohol intake indirectly by asking such questions as: do you drink before meals?; when you go to restaurants, do you stop at the bar before going to the dining room?; is the cocktail hour the best hour of the day?; during

the day do you think about the first drink to come?; when entertaining, do you take a private sip while fixing drinks for guests?; do you like to pour drinks for your guests?; how much alcohol do you keep in your home, or your office?; is alcohol a conversation topic at home?; have you ever been drunk?; have you ever gotten drunk because of anger or frustration?

There is a large gray area between the social drinker who never becomes alcoholic and the alcoholic who is passing through the early phase, but in many cases the symptoms plus the patient's answers to the questions will provide an identifiable pattern, Dr. Davis says.

---

#### *JOGGING SAFER THAN RUNNING FOR MOST PERSONS*

CHICAGO - Running provides more exercise than jogging, but for the average person jogging is a much safer activity, says an expert on sports medicine in the July 11 Journal of the American Medical Association.

The exertion of jogging is slightly more than that of walking, and slightly less than that of running, Allan J. Ryan, MD, of Edina, Minn., points out.

The function of the heart muscle can be improved only by overloading it, Dr. Ryan emphasizes. Thus the more strenuous the exercise, the more activity is required of the heart. A person engaged in running can get closer to his maximum capacity than the jogger.

But, to achieve substantial benefits from exercise, the average person does not need to get very close to maximum capacity, he says.

"From the standpoints of comfort and safety and assuming proper footwear is worn, that adequate warm-up exercises are performed, and that a moderately resilient running surface is used, jogging is a much safer activity for the average person than running.

"There is no question, however, that the sensation experienced with running is more pleasurable and rewarding than that obtained in jogging, but musculoskeletal problems are more frequent and are apt to be more severe with running."

*EMERGENCY MEDICINE EMERGES AS NEW SPE-*

## CIALTY

CHICAGO — A new specialty area has emerged in American medicine in recent years — emergency medicine.

Because of an explosive increase in the use of emergency rooms in hospitals across the country, many hospitals have found it expedient to employ full-time emergency physicians, says a report in the July 11 Journal of the American Medical Association.

The demand for emergency physicians has prompted the development of training programs in emergency medicine in academic medical centers. Alton I. Sutnick, MD, and David K. Wagner, MD, of the Medical College of Pennsylvania, Philadelphia, report on the growth of these training programs.

Begun in 1970 at the University of Pennsylvania, formal postgraduate training programs in emergency medicine are now offered in 32 institutions in the United States and Canada. The American College of Emergency Medicine Physicians was established, and now has some 9,000 members. An American Board of Emergency Medicine has been formed and is now

developing criteria for certification of specialists.

The emergency physician must have training to recognize and respond competently to severe situations, be prepared to take decisive, life-saving actions, and be a leader in helping develop community emergency medical systems, say Drs. Sutnick and Wagner.

His training includes a broad range of disease processes as well as knowledge of the health provision system, awareness of social agencies, and the ability to function with community groups. He must know something of the traditional specialties of internal medicine, surgery, pediatrics, obstetrics and gynecology, and psychiatry. He also must engage in teaching and research.

The field currently suffers from a major disadvantage, in that physicians of other specialties tend to feel they can collectively provide emergency service, they say. There is now under way a concerted attempt to define the body of knowledge and characteristics that might be considered unique to the field of emergency medicine.

## LISTA DE ANUNCIANTES

- |                          |                           |
|--------------------------|---------------------------|
| 1. BURROUGHS WELLCOME    | CODEINE ANAL.             |
| 2. CIBA PHARM.           | VIOFORM - HC              |
| 3. PENNWALT CORP.        | ZAROXOLYN                 |
| 4. PHARMACEUTICAL MFG.   | INSTITUTIONAL             |
| 5. ROCHE LAB.            | GANTANOL, LIBRIUM, VALIUM |
| 6. ROERIG & CO.          | ANTIVERT                  |
| 7. W. H. RORER           | CAMALOX                   |
| 8. SMITH, KLINE & FRENCH | DYAZIDE                   |





## Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

■ **Most Widely Prescribed**—Antivert is the most widely prescribed agent for the management of vertigo\* associated with diseases affecting the vestibular system such as Menière's disease, labyrinthitis, and vestibular neuronitis.

■ **Relief of Nausea and Vomiting**—Antivert/25 can relieve the nausea and vomiting often associated with vertigo\*.

■ **Dosage for Vertigo\***—The usual adult dosage for Antivert/25 is one tablet t.i.d.

### BRIEF SUMMARY OF PRESCRIBING INFORMATION

**\*INDICATIONS.** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

**Effective:** Management of nausea and vomiting and dizziness associated with motion sickness.

**Possibly Effective:** Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

**CONTRAINDICATIONS.** Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

**WARNINGS.** Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.


**Usage in Children:** Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

**Usage in Pregnancy:** See "Contraindications."

**ADVERSE REACTIONS.** Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

**ROERIG**   
A division of Pfizer Pharmaceuticals  
New York, New York 10017

**Antivert<sup>®</sup>/25**   
(meclizine HCl) 25 mg. Tablets  
**for vertigo\***





**Only 1  
tablet B.I.D.**

**New convenience**  
**Gantanol<sup>®</sup> DS**  
sulfamethoxazole/Roche  
**double-strength dosage form  
for acute cystitis\* patients**

\*nonobstructed; due to susceptible organisms

New Gantanol® DS (sulfamethoxazole) tablets offer even greater convenience and economy for your patients with acute, unobstructed cystitis due to susceptible strains of *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*... The same amount of medication, the same efficacy, with only *half* the number of tablets per day. Simplified dosage regimen encourages patient compliance: 2 tablets (1 Gm each) STAT—then 1 tablet B.I.D. for 10 to 14 days. Clinical efficacy so basic you can start cystitis therapy even before culture results are available.

• In a clinical study of 406 patients on Gantanol (sulfamethoxazole) B.I.D., close to 9 out of 10 patients achieved negative urine cultures. While Gantanol tablets were used in this study, one Gantanol DS tablet has been proved bioequivalent to two Gantanol tablets.\*

Gantanol is contraindicated during pregnancy, during the nursing period, and in infants under 2 months. During therapy, maintain adequate fluid intake, perform frequent CBC's and urinalyses with careful microscopic examination.

\*Data on file, Hoffmann-La Roche Inc., Nutley, New Jersey.

# and economy

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Acute, recurrent or chronic urinary tract infections (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*), in the absence of obstructive uropathy or foreign bodies. Note: Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides, especially in chronic or recurrent urinary tract infections. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Sulfonamide hypersensitivity; pregnancy at term and during nursing period; infants less than two months of age.

**Warnings:** Safety during pregnancy has not been established. Sulfonamides should not be used for group A beta-hemolytic streptococcal infections and will not eradicate or prevent sequelae (rheumatic fever, glomerulonephritis) of such infections. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy. Insufficient data on children under six with chronic renal disease.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, epidermal necrolysis, urticaria, serum sickness,

pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *gastrointestinal reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L.E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia as well as thyroid malignancies in rats following long-term administration. Cross-sensitivity with these agents may exist.

**Dosage: Systemic sulfonamides are contraindicated in infants under 2 months of age** (except adjunctively with pyrimethamine in congenital toxoplasmosis). *Usual adult dosage:* 2 Gm (2 DS tabs or 4 tabs or 4 teasp.) initially, then 1 Gm *b.i.d.* or *t.i.d.* depending on severity of infection.

*Usual child's dosage:* 0.5 Gm (1 tab or teasp.)/20 lbs of body weight initially, then 0.25 Gm/20 lbs *b.i.d.* Maximum dose should not exceed 75 mg/kg/24 hrs.

**Supplied:** DS (double strength) tablets, 1 Gm sulfamethoxazole; Tablets, 0.5 Gm sulfamethoxazole; Suspension, 0.5 Gm sulfamethoxazole/teaspoonful.

**Basic therapy with convenience and economy:**

**Gantanol®** (sulfamethoxazole)Roche®

**Basic therapy with even more convenience and economy:**

**Gantanol® DS** (sulfamethoxazole)Roche®



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

# TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE **DYAZIDE®**

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### \* Warning

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

\* **Indications:** When the combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium sparing action of triamterene is warranted. (See Box Warning.) Routine use of diuretics in healthy pregnant women is inappropriate; they are indicated in pregnancy only when edema is due to pathological causes.

**Contraindications:** Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum  $K^+$  levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict  $K^+$  intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids).

Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum  $K^+$  frequently; both can cause  $K^+$  retention and elevated serum  $K^+$ . Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis.

'Dyazide' interferes with fluorescent measurement of quinidine.

### Adverse Reactions:

Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions;

nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

SK&F CO., Carolina, P.R. 00630

**FOR LONG-TERM CONTROL  
OF HYPERTENSION\*  
SERUM  $K^+$  AND BUN SHOULD  
BE CHECKED PERIODICALLY.  
(SEE WARNINGS SECTION.)**

**SK&F CO.**  
a SmithKline company



# ASOCIACION MEDICA DE PUERTO RICO

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

DEC 14 1977



1902 — 1977

75to. ANIVERSARIO

**VOL. 69**

**Septiembre 1977**

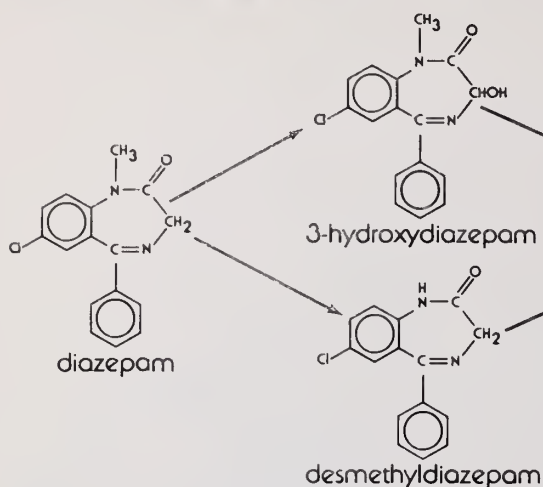
**No.9**

PLAY  
LIVES

**BOLIVIA**

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE

# A pharmacokinetic character all its own



**Valium (diazepam) is a benzodiazepine with a distinctive pharmacokinetic profile**

The pharmacokinetic profile of Valium is one of the characteristics that sets it apart from other benzodiazepines. Consider, in particular, the metabolic pathway of Valium. The three major metabolites of Valium exhibit significant pharmacologic activity—and so, of course, does the parent substance—diazepam itself. All combine to produce the characteristic clinical response seen with Valium. The response you have come to know, to want and to trust.

Pharmacokinetic studies also demonstrate that Valium has a pattern of absorption, distribution, metabolism and elimination that is reliable and consistent. And, although the pharmacokinetics of a drug cannot, at present, be specifically related to its clinical effects, it is clearly a factor that distinguishes one product from another by providing important insights into how each moves through the patient's body.

## Valium® (diazepam) <sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma;

may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

Upjohn

# Orinase

tolbutamide, U.S.P., Upjohn

0.5 Gm tablets





**anti-inflammatory**

**antipruritic**

**antibacterial**

**antifungal**



# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform® Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm. **Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of ½ and 1 ounce. **Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/6870 17

# Vioform® Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

# ASOCIACION MEDICA DE PUERTO RICO

Organo Oficial

Fundado en 1903

Volumen 69

Septiembre 1977

Número 9

## JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bermúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

TODO MATERIAL SOMETIDO A ESTA PUBLICACION DEL BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO PUEDE SER FOTOCOPIADO PARA PROPOSITOS EDUCACIONALES Y CIENTIFICOS NO COMERCIALES.

## Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

## Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

## Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Post Operative Electrocardiographic Changes After Ventricular Aneurysmectomy .....	281
Juan M. Aranda, MD, Stanley Richter, MD, Benjamín Befeler, MD and Nabil El-Sherif, MD	
Herencia vs. Ambiente en Diabetes Mellitus Revisión y Conceptos Propios .....	290
Adolfo Pérez Comas, MD, PhD	
Cardiac Pacemaker Therapy During Pregnancy Labor and Delivery for Heart Block .....	297
Charles D. Johnson, MD	
The Cat-Cry Syndrome, an Unusual Chromosomal Aberration: Report of a Case and Review of the Literature .....	303
Fermín Sánchez Lugo, MD, José M. García-Castro, MD and Luz Carlota Reyes de Torres, MS	
Graphics .....	308
Juan M. Aranda, MD	
Editorial: Diabetes Mellitus: ¿Herencia o Ambiente?.....	311
Francisco Aguilo, Jr.	
Noticias .....	313



## POST OPERATIVE ELECTROCARDIOGRAPHIC CHANGES AFTER VENTRICULAR ANEURYSMECTOMY

Juan M. Aranda, MD, Stanley Richter, MD, Benjamín Befeler, MD and Nabil El-Sherif, MD

**Summary:** Electrocardiographic (ECG) changes after left ventricular aneurysmectomy were analyzed in 20 patients; thirteen of whom had additional aorto-coronary saphenous vein bypass surgery. ECG changes were correlated with post-operative clinical and hemodynamic results. Out of 14 patients (Group I) who showed hemodynamic and/or clinical improvement 8 had decrease of chronic ST segment elevation that was associated in 5 with loss of pathologic Q waves. In the remaining 6 patients (Group II) who showed no hemodynamic and/or clinical improvement as well as in 6 patients in Group I, chronic ST segment elevation persisted or increased and in some, loss of pathologic Q waves developed after surgery. The study suggests that loss of pathologic Q waves and/or decrease of chronic ST segment elevation in patients who undergo a left ventricular aneurysmectomy with aorto-coronary saphenous vein bypass surgery, may reflect postoperative clinical, hemodynamic and angiographic improvement. On the other hand, failure of these ECG changes to occur or conversely, increased ST segment elevation and/or appearance of new Q waves may have no predictive value. The mechanisms for these ECG changes are discussed.

The salient features of the electrocardiogram (ECG) in patients with left ventricular aneurysms have been extensively described (1-13). Although several ECG features have been reported, it is generally accepted that pathologic Q waves associated with persistent ST segment elevation appear to be the most specific; however, relatively little information is available concerning electrocardiographic changes after left ventricular aneurysmectomy. Accordingly, we systematically analyzed these changes in 20 patients and attempted to correlate them with clinical and hemodynamic findings.

### Methods

Twenty patients with surgical confirmation of left ventricular aneurysms who survived ventricular reconstruction during the years 1971-1973 are the subject of this study. The indications for surgery were: angina pectoris and/or congestive heart failure in 18 patients; 17 were refractory to medical therapy (Class III and IV, New York Heart Association criteria). Two patients underwent surgery for recurrent ventricular tachycardia.

The clinical status was determined by outpatient interview and physical examination. Follow up period was 7 to 43 months (mean 22 months) after surgery. Post-operative cardiac catheterization and arteriography was performed in 8 patients. Hemodynamic studies were analyzed and changes in angiographically determined wall motion abnormalities were recorded using standard techniques previously described (14).

Thirteen patients had, in addition to left ventricular aneurysmectomy, one or more coronary bypass

---

*From the Cardiovascular Laboratory, Cardiology Section, Veterans Administration Hospital, University of Miami School of Medicine, Miami, Florida, and the Cardiology Service, Veterans Administration Hospital, San Juan, Puerto Rico.*

*Request reprints to: Juan M. Aranda, MD, Veterans Administration Hospital, San Juan, P. R. 00936.*

TABLE I  
CLINICAL DATA

Case	Age (Years)*	Follow Up + Months	Site of Aneurysm $\phi$	Site of ACB	CLINICAL ASSESSMENT	
					Pre-Op Functional Class	Post-Op Functional Class
1	47	13	anteroapical		III (CHF)	(U) III (CHF)
2	60	8	anteroapical		I §	(I) no VT
3	53	11	anteroapical	RPD	IV (A)	(I) I
4	54	36	inferior posterior	RPD, LVB	IV (CHF)	(I) II (CHF)
5	55	30	anterolateral		III (A)	(I) II (A)
6	45	41	anterolateral	RPD, OM	IV (A&CHF)	(I) II (A&CHF)
7	51	7	inferior & apex		IV (A)	(I) II (A)
8	49	21	anteroapical	RPD, OM	IV (A), III (CHF)	(I) II (A&CHF)
9	64	15	inferior & apex	RPD	IV (A), III (CHF)	(I) II (A&CHF)
10	53	39	anteroapical	RPD,LAD	IV (CHF), II (A)	(I) I
11	54	12	anteroapical	RCA	IV (A), III (CHF)	(U) IV (A), III (CHF)
12	66	31	anteroapical	RCA	IV (A)	(I) II (A)
13	66	16	inferior and apex	OM	III (CHF)	(I) I
14	63	13	inferior & apex	RPD,OM,LAD	IV (A), II (CHF)	(U) IV (A), III (CHF) expired from cerebral embolus
15	61	3	apex & anterolateral	RPD,OM	IV (CHF)	(U) IV (CHF) expired from cardiac arrest & acute tubular necrosis
16	37	14	infero-posterior	RCA	II (CHF)	(I) I
17	74	14	inferior		II (CHF) §	(U) II (CHF)
18	64	25	anterolateral	LAD,OM	IV (A), II (CHF)	(I) II (A&CHF)
19	72	3	anterolateral & apex		IV (CHF)	(U) IV (CHF)
20	56	43	antero-apical posterior		III (A)	(I) II (A)

\* Age is given for patients at the time surgery performed

+ Time from surgery to latest clinical re-assessment

 $\phi$  Aneurysm location determined by operative report. If report was unavailable location was determined by pre-operative LV angiogram.

§ Indication for surgery was recurrent ventricular tachycardia

(I) = Improved, (U) = unimproved, (A) = angina, (CHF) = congestive heart failure. Roman numerals refer to New York Association Functional Classification. ACB = aortocoronary bypass, RPD = right posterior descending artery, RCA = right coronary artery, OM = obtuse marginal artery, LAD = left anterior descending artery, LVB = left ventricular branch, VT = ventricular tachycardia.

grafts for obstructive coronary arterial lesions.

Electrocardiograms were reviewed by two independent observers who were unaware of the patients' clinical assessment. Only ECG with satisfactory technical quality, especially in relation to standardization and correct placement of precordial electrodes, were analyzed. Because of the sensitivity of ST-T segment to heart rate, only tracings with a heart rate of 60-90 beats/minute were studied.

Representative pre-operative and post-operative ECG were analyzed by the same observers. Post-operative ECG obtained at least one month following surgery were analyzed to avoid transient acute changes secondary to the surgical stress. All ECG were systematically analyzed for rhythm, frontal plane QRS axis, PR intervals, QRS duration and the presence of bundle branch block pattern. Patients with complete left bundle block were excluded. ST elevation was defined as greater than 1 mm elevation of the mid-portion of the ST segment (regardless of contour) above the base line defined by successive T-P segments. The sum of ST elevation in the standard 12-lead ECG was calculated for each patient. Pathologic Q waves (duration > 0.04 sec.) were noted, as well as the presence of both Q waves and ST segment elevation in the same leads. Statistical analysis was performed using the Chi Square test.

## Results

Table I summarizes pertinent clinical data in 20 patients with left ventricular aneurysmectomy. The table includes the site of aorto-coronary saphenous vein bypass grafts in 13 of the 20 patients who underwent this operation. A summary of ECG data is shown in Table II. All patients were men with age ranging from 37 to 74 years (mean of 57.2 years).

The aneurysm involved the apex and anterior wall in 17 of 20 patients. All but 3 of these 17 patients had pathologic Q waves as evidence of prior transmural anterior myocardial infarction. Four patients also had Q waves involving the inferior leads. Of the 3 patients in whom the aneurysm did not involve the anterior wall, one (case 16) had electrocardiographic criteria for true posterior infarc-

tion and had no Q waves. The other patients (cases 4 and 17) with inferior wall aneurysm demonstrated Q waves in inferior leads (II, III, and AVF).

Persistent S-T segment elevation was present in either the anterior precordial or inferior limb leads in 18 of 20 patients (90 percent). Two patients with aneurysms involving the apex did not have ST segment elevation. In these patients (cases 7 and 11) the aneurysm was localized to the infero-apical and antero-apical wall respectively.

## *Correlation of Functional ECG Changes:*

On the basis of post-operative clinical evaluation, patients were classified in two groups. Group I included 14 patients who experienced clinical improvement following surgery (change of at least one functional class by New York Heart Association criteria). Group II consisted of 6 patients who showed no clinical improvement. In Group I the aneurysms were anterior in 9, and inferior in 5. Absolute quantitation of pre-operative ST segment elevation ranged from 0 to 11.5 mm with an overall mean for the entire group of 6.4 mm. Eight of the 14 patients had a decrease in ST segment elevation, (Figures 1 and 2). All of these patients had concomitant coronary bypass surgery. In 3 patients, ST segment elevation increased and in 3 no change occurred.

The post-operative mean ST segment elevation for Group I was 4 mm, compared to 6.4 mm in the pre-operative ECG. The difference was statistically significant ( $p < .02$ ). In 6 of 14 patients in Group I (43 percent), there was loss of pathologic Q waves in one or more leads (Figures 3 and 4). All patients had coronary bypass surgery. Two patients developed new Q waves and in 6, the Q waves remained unchanged.

Aneurysm location in Group II was anterior or apical in 4; inferior in 1, and combined in another. In none of the Group II patients



TABLE II  
ELECTROCARDIOGRAPHIC DATA - PREOPERATIVE AND POSTOPERATIVE CHANGES

Case	Rhythm		Axis		QRS Duration		Conduction Disturbance		Quantitation of STE (MM)		Pre-Op Location of Pathologic Q Waves	Post-Op Changes in Q Waves
	Pre-Op	Post-Op	Pre-Op	Post-Op	Pre-Op	Post-Op	Pre-Op	Post-Op	Pre-Op	Post-Op		
1	NSR	NC	-18°	-10°	.09	.10	IVCD	NC	5.5	5.5	I,AVL,V1-4	NC
2	NSR	NC	+90°	-35°	.08	.12	LAH-IVCD	LAH-IVCD	1.0	5.5	V1-5	New in I,AVL,V6
3	NSR	NC	-50°	-50°	.10	.09	LAH-IVCD	NC	5.0	2.0	I,AVL,V2-6	Absent in AVL,V2
4	NSR	NC	0°	0°	.08	.10	IVCD	IVCD	2.5	6.0	II,III,AVF,V6	Absent in II,V6
5	NSR	NC	-60°	-60°	.08	.08	LAH	NC	4.5	7.5	V1-6	New in II,III,AVF
6	NSR	NC	-135°	-90°	.10	.11	LAH-IVCD	NC	11.5	2.5	I,AVL,V1-5	Absent in I,AVL
7	AFB	NC	+35°	0°	.08	.08			0	0	None	NC
8	NSR	NC	+70°	+60°	.10	.10	IVCD	NC	6.0	4.0	I,II,AVL,V2-6	Absent in II,V2
9	NSR	NC	-10°	-75°	.08	.10	LAH-IVCD	LAH-IVCD	7.0	7.0	AVL,V1-4	NC
10	NSR	NC	-50°	-30°	.12	.12	IVCD	NC	7.0	2.0	II,III,AVF,V3-6	NC
11	NSR	NC	-40°	-40°	.08	.08	LAH	NC	0	0	III,AVF	New in II,III
12	NSR	NC	-10°	0	.10	.09			5.0	1.0	I,AVL,V3-5	Absent in I,V3-5
13	NSR	NC	+120°	+90°	.11	.11			10.0	1.0	V4-6,II,III,AVF	NC
14	SB	ST	-70°	-75°	.11	.08	LAH-IVCD	LAH-NO IVCD	3.5	4.5	II,III,AVF,V1-6	NC
15	NSR	AF	-60°	-60°	.10	.10	1°AV block LAH	NC	7.5	10.5	III,AVF,V1-4	NC
16	NSR	NC	-40°	-75°	.09	.09	LAH-IRBBB	NC	8.0	8.0	None	NC
17	NSR	NC	-40°	-40°	.10	.10	LAH-IRBB	NC	1.5	4.0	III,III,AVF	NC
18	NSR	ST	-40°	-40°	.10	.10	LAH-IVCD	NC	9.0	7.0	V1-3	Absent in V1-3
19	AFB	NC	-55°	-55°	.16	.16	LAH-RBBB	NC	9.5	10.5	AVL,V1	NC
20	NSR	NC	-40°	-40°	.10	.10	LAH	NC	6.5	2.5	None	NC

ABBREVIATION: NSR = Normal Sinus Rhythm; AFB = Atrial fibrillation; SB // sinus bradycardia; ST = sinus tachycardia; AF = atrial flutter; NC = no change; LAH = left anterior hemiblock; IVCD = intraventricular conduction delay; IRBBB = incomplete right bundle branch block; RBBB = right bundle branch block; STE = ST segment elevation.

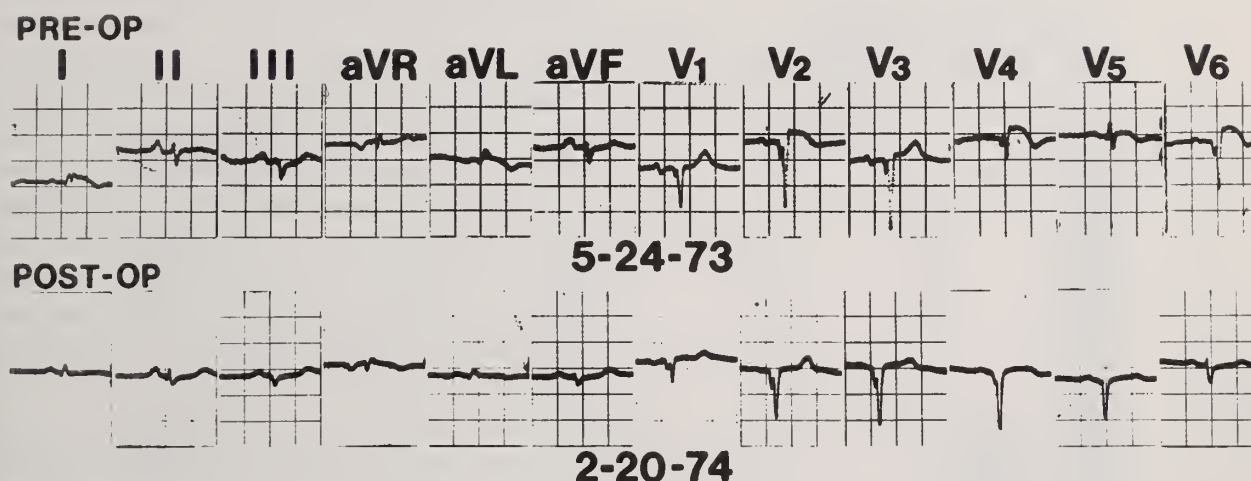


Figure 1, Case 10 — Electrocardiogram taken before and after aneurysmectomy revealed decrease in chronic ST segment elevation (I, aVL, V<sub>1</sub>-V<sub>6</sub>). Q waves remained unchanged.

did the post-operative ECG show a decrease in ST segment elevation. In contrast, 4 of 6 patients had an increase of ST segment elevation. Three of these patients had aorto-coronary saphenous vein bypass. The mean pre-operative ST segment elevation in Group II was 4.6 mm and increased to 6 mm after surgery. The change was not statistically significant ( $p > .05$ ). In addition, none of the 6 patients showed loss of pathologic Q waves following surgery.

Table III shows the results of post-operative hemodynamic studies in 8 patients. All seven cases from Group I demonstrated improved segmental contractility (dyskinetic areas became hypokinetic). Five of the 7 patients showed rise in cardiac indices and 4 had either normalization or decrease of a pre-operative elevated end-diastolic pressure. The only patient studied from Group II had a persistent dyskinetic area in the antero-apical wall with no change in the cardiac index. This patient (Case 11) also showed a new pathologic Q wave in lead II following surgery. Of the seven Group I patients studied hemodynamically, five had a decrease in chronic ST segment elevation and four

had loss of pathologic Q waves. The other patient studied (Group II) with no clinical or hemodynamic evidence of improvement had neither loss of Q waves nor a decrease in ST segment elevation.

### Discussion

The incidence of chronic ST elevation in patients with left ventricular aneurysms has varied in different series partly related to the criteria used for the diagnosis of ventricular aneurysm. The incidence is usually higher in autopsy series in which definite external protrusion of scar tissue was required for diagnosis. It is usually lower in angiographic series in which highly variably proportions of scar and muscle were demonstrated in the areas of ventricular asynergy (15). The incidence of ST segment elevation in this series (90 percent) is higher than most of the reported series which averages 64 percent (16). Although persistent elevation of ST segment is an insensitive index of ventricular aneurysm, recent studies suggest that it may be highly specific. Thus, Burr and

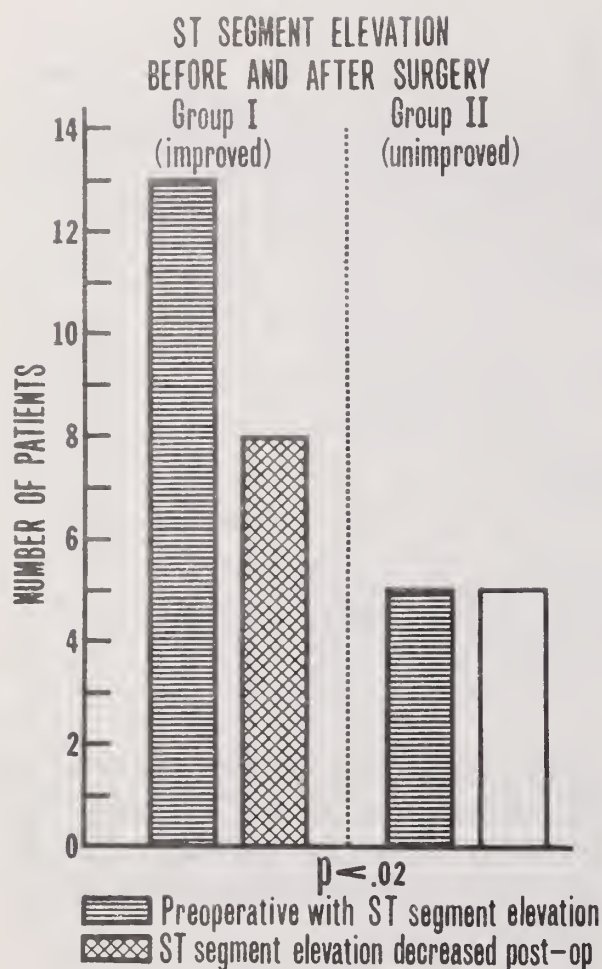


Figure 2 — Relationship between clinical improvement and decrease of chronic ST segment elevation after ventricular aneurysmectomy. Only 13 group I patients and 5 group II patients showed persistent ST segment elevation before the operation.

Iseri (17) demonstrated left ventricular aneurysm by cineangiography in all 24 patients in whom 2 mm of ST elevation persisted for 3 weeks post-myocardial infarction in two or more ECG leads. Mills and co-workers (16) have demonstrated that ST segment elevation greater than 1 mm two weeks after infarction is a highly specific index of advanced asynergy.

There is little information available concerning the electrocardiographic response to surgical

repair of left ventricular aneurysm. Lillehei and co-workers (18) reviewed three cases and did not report any significant ECG changes. More recently, Thind, Blackmore et al (19), described a patient who underwent aneurysmectomy for intractable ventricular tachycardia. In this case, the post-operative electrocardiogram remained unchanged with persistent Q waves and ST segment elevation across the anterior precordial leads. In another case reported by Gallagher, Oldhama and Wallace (20), the electrocardiogram was shown unchanged following aneurysmectomy.

The present study demonstrated for the first time the prevalence of significant ECG changes following left ventricular aneurysmectomy associated with aorto-coronary saphenous vein bypass. Thus, 8 of 20 patients (40 percent) with combined ventricular aneurysmectomy and coronary bypass grafts had a decrease in chronic ST segment elevation with loss of pathologic Q waves in 5. The remaining patients showed either no change or an increase in chronic ST elevation, as well as no change in pathologic Q waves or the development of new Q waves. Of particular significance is the association of the decrease of ST segment elevation and the loss of pathologic Q waves in the postoperative ECG with clinical hemodynamic and angiographic evidence of improved left ventricular performance.

The mechanism of chronic ST segment elevation in ventricular aneurysm is not fully elucidated. This probably also applies to ECG changes following left ventricular aneurysmectomy and coronary bypass surgery described in this report. Many theories have been proposed for the etiology of chronic ST segment elevation associated with ventricular aneurysm. Moyer and Hiller (21) suggested that this may be due to lack of modifying potentials from completely infarcted muscle associated with hypertrophy of the opposite wall. Overlapping of the process of repolarization and depolarization (22), and injury of junctional normal musculature resulting from mechanical trauma incident to the pulling and stretching of the



TABLE III  
CATHETERIZATION DATA

Case	Site of Abnormal Wall Motion	Group	Change in Wall Motion	C. I.		Change in LVEDP	
				Pre-Op	Post-Op	Pre-Op	Post-Op
2	anteroapical	I	$D \approx H$	2.7	2.7	16	12
3	anteroapical	I	$D \rightarrow H$	2.3	2.9	22	16
4	inferolateral	I	$D \rightarrow H$	2.7	2.8	27	19
6	anterolateral	I	$D \rightarrow H$	2.5	3.7	9	18
10	anteroapical	I	$D \rightarrow H$	1.6	3.9	19	20
11	anteroapical	II	$D \rightarrow D$	2.4	2.3	10	27
12	anteroapical	I	$D \rightarrow H$	1.8	2.4	6	8
13	apex & inferior	I	$D \rightarrow H$	2.6	3.6	26	16

ABBREVIATIONS: D = dyskinctic, H = hypokinetic

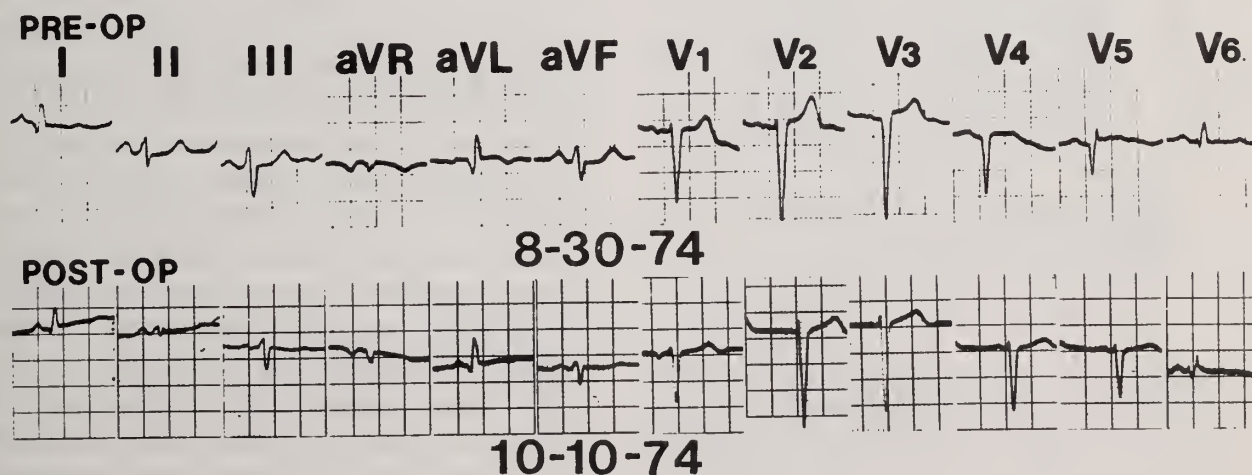


Figure 3, Case 12 — Electrocardiograms taken preoperatively and after aneurysmectomy revealed loss of pathologic Q waves in  $V_3$  through  $V_5$ . Q waves in leads I and AVL are less prominent. There was no significant change in frontal plane axis.

rim of the aneurysmal sac, have also been postulated (23). The decrease of chronic ST elevation observed in some patients following resection of the ventricular aneurysm may be ascribed to the effect of successful removal of an area of predominantly fibrotic scar. This

may have helped to alleviate the interface of fibrotic tissue on normal myocardium that may be operative in the genesis of chronic ST segment elevation. The observation that post-operative decrease of chronic ST segment elevation was only seen in patients who demonstra-

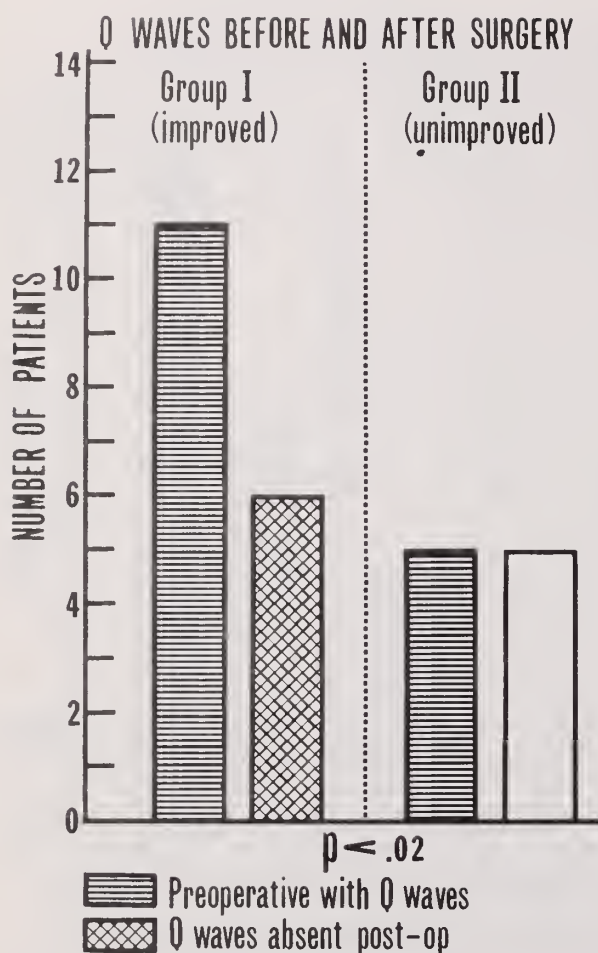


Figure 4 — Relationship between clinical improvement and disappearance of Q waves after ventricular aneurysmectomy. Only 11 group I patients and 5 group II patients showed pre-operative pathologic Q waves.

ted clinical, hemodynamic, and angiographic improvement may suggest that in these patients most of the predominantly fibrotic tissues have been excised. Conversely, patients who were left with sizable areas of predominantly fibrotic myocardium even after the excision of the aneurysmal sac may not be expected to show clinical or angiographic improvement and chronic ST segment elevation may persist.

During surgery of ventricular aneurysm

it may be sometimes difficult to identify diffuse areas of fibrotic scar tissue interspaced with normal myocardium. Thus, the surgeon's operative note may not be sufficient to predict which patient may show improvement following ventricular aneurysmectomy. All patients who showed a postoperative decrease of chronic ST segment elevation had coronary bypass surgery. Although grafts were not usually constructed in areas of previous scar tissues, revascularization of previous ischemic myocardium can conceivably alter the ST segment by a process of summation and cancellation (21).

The mechanism for loss of pathologic Q waves in some patients following resection of ventricular aneurysm and coronary bypass grafts is more difficult to explain. Several factors may be operative. According to classic electrocardiographic concepts Q waves are caused by transmission of negative left ventricular cavity potentials through a "window" of dead muscle (23). It is conceivable, according to this concept, that excision of the aneurysmal scar tissue would result in loss of pathological Q waves in leads facing the site of the original aneurysm. However, the "window" theory has been recently reappraised, and it is now generally appreciated that transmural myocardial infarction is not an electrophysiologic requirement for pathologic Q waves (24). Some evidence suggests that loss of electromotive force can occur without irreparable cell death (25). Coronary bypass surgery has been reported to result in either regeneration of electromotive force lost following infarction (26) or the appearance of new post-operative Q waves due to unmasking of an old infarction (27). Both changes in the ECG have been explained on improvement of chronically ischemic myocardium upon re-establishment of adequate perfusion. One further mechanism that can result in appearance or disappearance of pathologic Q waves is a change in intraventricular conduction (28) which was observed in some patients in the present series.

In summary, the present study suggests that loss of pathologic Q waves and/or decrease of chronic ST segment elevation in patients who undergo left ventricular aneurysmectomy and coronary bypass surgery may reflect post-operative clinical, hemodynamic and angiographic improvement. On the other hand, failure of these ECG changes to occur or conversely, worsening of ST segment elevation and/or appearance of new Q waves may have not predictive value, since these changes were seen in patients who did or did not show clinical improvement.

### Acknowledgment

We would like to acknowledge the cooperation of Ms. Marisa González for the typewritten preparation of the manuscript, as well as Dr. Marcelino Obaya for the art work.

### References

1. Parkinson, J., Bedford, D. E., Thomson, W. A. R.: Cardiac aneurysm, Q. J. Med. 7: 455, 1938
2. Nordenfelt, O.: The electrocardiogram in chronic aneurysm of the heart. Acta Med. Scand. 102: 101, 1939.
3. Scherf, D., Boyd, L. J.: Cardiac aneurysm. Med. Clin. North Am. 26: 919, 1942.
4. Wilson, F. N., Rosenbaum, F. F., Johnston, F. D.: Interpretation of the ventricular complex of the electrocardiogram. Adv. Intern. Med. 2: 1, 1947.
5. Myers, C. B., Klein, H. A., Hiratzka, T.: Correlation of electrocardiographic and pathologic findings in large anterolateral infarcts. Am. Heart J. 36: 838, 1948.
6. Zimdahl, W. T., Busurego, S.: Ventricular aneurysm: Report on two cases. Am. Pract. 3: 185, 1948.
7. Scherf, D., Brooks, A. M.: The murmurs of cardiac aneurysm. Am. J. Med. Sci. 218: 389, 1949.
8. Myers, C. B., Klein, H. A., Hiratzka, T.: Correlation of electrocardiographic and pathologic findings in anteroposterior infarction. Am. Heart J. 37: 205, 1949.
9. Rosenberg, B., Messinger, W. J.: The electrocardiogram in ventricular aneurysm. Am. Heart J. 37: 267, 1949.
10. Goldberger, E.: Unipolar Lead Electrocardiography, Lea and Febiger, Philadelphia, 1949 pp 220.
11. Laake, H.: Postinfarction myocardial aneurysm. Acta Med. Scand. 167: 221, 1960.
12. Dubnow, M. H., Burchell, H. B., Titus, J. L.: Post-infarction ventricular aneurysm. A clinicomorphologic and electrocardiographic study of 80 cases. Am. Heart J. 70: 753, 1965.
13. El-Sherif, N.: The RSR pattern in left surface leads in ventricular aneurysm. Brit. Heart J. 32: 140, 1970.
14. Herman, M. V., Heinle, R. A., Klein, M. D.: Localized disorders in myocardial contraction. N. Eng. J. Med. 277: 222, 1967.
15. Corlin, R., Klein, M. D., Sullivan, J. M.: Prospective correlative study of ventricular aneurysm. Amer. J. Med. 42: 512, 1967.
16. Mills, R., Young, E., Corlin, R., Lesch, M.: Natural history of S-T segment elevation after acute myocardial infarction. Am J Cardiol. 35: 609, 1975.
17. Burr, A. R., Karr, R. M., Iseri, L. T.: Reliability of the electrocardiographic signs of ventricular aneurysm. Circulation 46 (Suppl. II) 11, 1972.
18. Lillehei, C. W., Levy, M. J., DeWall, R. A.: Resection of myocardial aneurysms after infarction during temporary cardiopulmonary bypass. Circulation, 26: 206, 1962.
19. Thind, G. S., Blakemore, W. S., Zinsser, H. F.: Ventricular aneurysmectomy for the treatment of recurrent ventricular tachyarrhythmia. Am. J. of Cardiol. 27: 690, 1971.
20. Gallagher, J., Oldham, H., Wallace, A.: Ventricular aneurysm with ventricular tachycardia. Am. J. Cardiol. 35: 696, 1975.
21. Moyer, J. B., Hiller, G. I.: Cardiac aneurysm: Clinical and electrocardiographic analysis. Am. Heart J. 41: 340, 1951.
22. Grisham, A., Scherlis, L.: Spatial Vectocardiography, W. B. Saunders, Co., Philadelphia, 1952 pp 59.
23. Lipman, B., Massie, E.: Clinical Scalar Electrocardiography. Year Book Medical Publishers, Chicago 1972, pp 254.
24. Helfant, R. H.: Q waves in coronary heart disease: Newer understanding of their clinical implications. Amer. J. Cardiol. 38: 662, 1976.
25. Gross, H., Rubin, I. L., Laufer, H.: Transient abnormal Q waves in the dog without myocardial infarction. Amer. J. Cardiol. 14: 669, 1964.
26. Zeff, H. J., Friedberg, H. D., King, J. F.: Reappearance of anterior QRS forces after coronary bypass surgery. Amer. J. Cardiol. 38: 1963.
27. Bassan, M. M., Oatfield, R., Hoffman, I.: New Q waves after aortocoronary bypass surgery. Unmasking of an old infarction. New Engl. J. Med. 290: 349, 1974.
28. Leachman, R. O., Angelini, P., Lufschanowski, R.: Electrocardiographic signs of infarctions masked by coexisting centralateral hemiblock. Chest 62: 542, 1972.



## HERENCIA VS. AMBIENTE EN DIABETES MELLITUS REVISION Y CONCEPTOS PROPIOS

Adolfo Pérez Comas, MD, PhD

Múltiples han sido las teorías sobre el mecanismo causal en la diabetes sacarina. Por siglos ha sido conocida la agregación familiar de la condición. Richard Morton, en el Siglo XVII, fue el primero en especular sobre el factor hereditario de esta condición. Sin embargo, diversos estudios han mostrado un carácter familiar sugiriendo una gran probabilidad de predisposición genética. Es también conocido que, tanto factores ambientales como genéticos, pueden ser responsables de la agregación familiar.

El concepto de la herencia en la diabetes mellitus ha variado grandemente a través de los años, postulándose diversos tipos de herencia, sean estos de tipo autosómico recesivo, tipo dominante de penetración incompleta, o de tipo multifactorial.

La herencia autosómica recesiva, postulada por Pincus y White (2) en 1933, ha sido la más discutida. Ella implicaría que el sujeto afectado sería homocigótico para el gen en cuestión, existiendo riesgos específicos para los hijos de padres portadores, los hermanos en caso de gemelos idénticos, y naturalmente para los hijos de padres afectados (Fig. 1).

Herencia	AR- Riesgos
Ambos padres afectados	Riesgo de tener la condición 100% de hijos
1 gemelo idéntico afectado	hermano idéntico 100%
Ambos padres portadores	25% hijos

Figura 1

Estas cifras de riesgo no han sido confirmadas a cabalidad en estudios posteriores, incluyendo estudios de gemelos monocigóticos y dicigóticos (Fig. 2). Los resultados han sido variables, debido a los métodos de estudio utilizados (orina, sangre, estudios anatómopatológicos, etc.) al igual que el período de seguimiento (3) y el momento de aparición de la diabetes (Fig. 3).

Cambridge (4-5) en 1928 y 1934, en Inglaterra, postuló que en la diabetes temprana la herencia era autosómica recesiva y en la tardía autosómica dominante. Varios autores respaldaron este patrón de herencia, (6-8) hasta que Steinberg (9) lo refutó al no poder demostrar que la incidencia de diabetes en los padres de diabéticos de comienzo temprano era menor que en los padres de diabéticos de aparición tardía.

*Del Departamento de Genética Médica y Sección de Endocrinología Pediátrica - Hospital Dr. Ramón Emeterio Betances, Centro Médico de Mayagüez, Mayagüez, Puerto Rico.*

*Conferencia de Clausura del III Congreso Latinoamericano de Diabetes, Mayo 13-19, 1977, Lima, Perú.*

CONCORDANCIA EN DIABETICOS		
Estudio	Gemelos	
	Monocigóticos	Dicigóticos
Steiner	96.6%	9.1%
Harvald & Hauge 1963	73 %	32 %
White 1965	48 %	3 %

Figura 2

CONCORDANCIA EN GEMELOS IDENTICOS DIABETICOS			
AÑOS SEGUIMIENTO	%		% DE CONCORDANCIA GEMELOS <DE 45 AÑOS
	TODOS	(Dg.)	
0 - 3	52		42
3 - 10	78		56
11 - 20	92		69
21 - 30	—		82

Figura 3

Simpson (10) en 1969 y Neel (11) y asociados en 1969, presentaron datos que respaldan una herencia de tipo poligénica o multifactorial. Basan sus hallazgos en estudios de tolerancia de glucosa en una población de Michigan, en Norteamérica, cuyos datos al trazarse en una curva presentan una distribución uniforme, en forma de campana de Gauser o curva normal, y no bimodal como se observaría en un patrón recesivo.

Bennett y colaboradores (11) en un estudio poblacional con los indios Pima, observaron una elevada incidencia de diabetes y una curva de distribución bimodal por encima de los 25 años de edad, sugiriéndoles un patrón recesivo al grupo.

Al igual que en los humanos, en diversas especies animales hay divergencia en cuanto a patrones de herencia de hiperglicemia y diabetes mellitus. Así se ha observado por ejemplo que en el ratón (*Mus musculus*) hay seis genes mutantes distintos, algunos de los cuales se transmiten en forma recesiva, otros en forma dominante, y otros se comportan como multifactoriales (13).

De aplicar esto al hombre, respaldaría la hipótesis de que la diabetes es una condición genética heterogénea. Apoyan esta hipótesis la delineación de más de 30 condiciones genéticas distintas donde hay intolerancia a los glúcidos (14). Existen algunas cepas de ratas y ratones, donde se presentan diversas formas de transmisión hereditaria de la diabetes.

Varios factores limitantes en el estudio de la herencia en el hombre son también válidos en el campo de estudio de la herencia en la diabetes sacarina. Entre ellos podemos anotar, siguiendo a Neel (15), que la frecuencia depende de la edad, que la interacción con múltiples factores ambientales dificulta su análisis, que existe una elevada probabilidad de heterogeneidad, que la naturaleza del defecto básico es desconocida, y finalmente que carecemos de criterios diagnósticos y marcadores genéticos específicos.

Al presente, los factores genéticos no explican de por sí, a cabalidad, el origen de la condición.

Factores Ambientales

Tanto los factores genéticos como los ambientales, o ambos, pueden ser responsables de la agregación familiar de una condición. Si tomamos

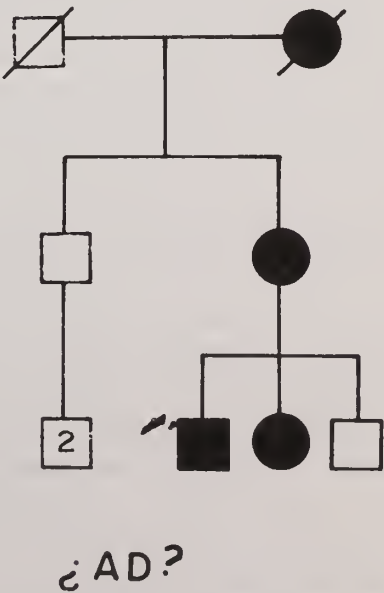


Figura 4

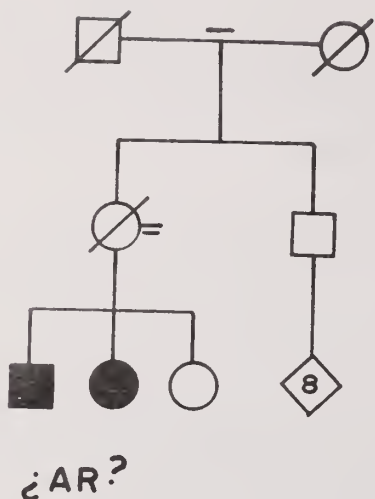


Figura 5

por ejemplo el árbol genealógico de esta familia (Fig. 4) observamos una transmisión de la condición de padres a hijos, lo que nos hace pensar en una herencia autosómica dominante. En esta otra familia (Fig. 5) observamos que la condición está presente en dos hermanas donde hay consanguinidad en los abuelos y los padres, lo que sugiere un patrón de herencia autosómica recesivo. Al investigar ambas familias más detalladamente encontramos (Figura 6) que ambas están relacionadas, y al ahondar más observamos que incluso la sirvienta y su hijo están afectados. Todos los afectados habitan y han habitado la misma residencia. Si nos guiáramos solo en el análisis de árboles genealógicos, indudablemente que podríamos caer en falsas interpretaciones, ya que lo que he mostrado aquí se trataba de una genealogía de tuberculosis pulmonar, enfermedad de indiscutible origen infeccioso en el que el ambiente juega un papel preponderante en su aparición. El estudio tan solo de árboles genealógicos puede llevar a confusiones (Fig. 7).

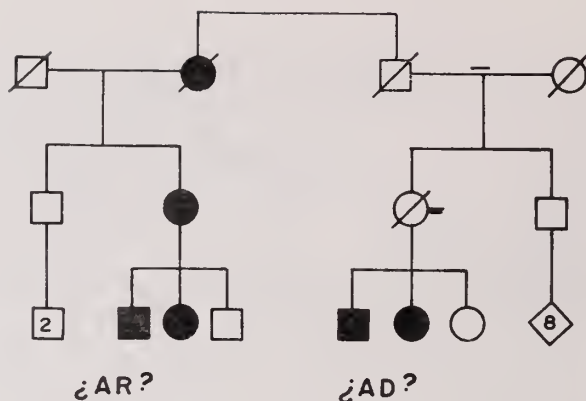


Figura 6

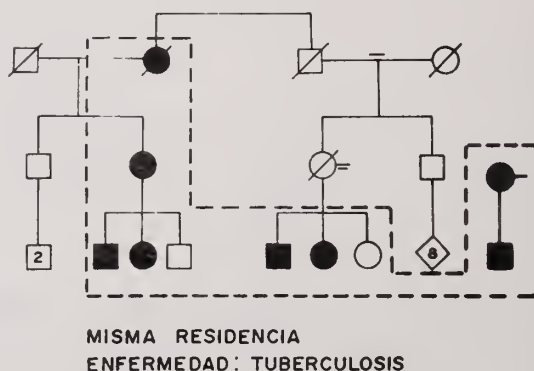


Figura 7

cionales, etc., podrían desempeñar un papel importante en la etiopatogenia de la diabetes sacarina.

Drásticamente saltamos aquí al concepto ambientalista que bien podría explicar la epidemiología de la diabetes mellitus. Factores dietéticos, de actividad física, infecciosos, emo-

Se ha dicho que la herencia carga el cañón, pero la obesidad y otros factores tiran del gatillo (16). Es indiscutible que la obesidad, como resultado de la extrimación dietética es un factor descompensador de importancia en la diabetes. Son muy conocidos los estudios de períodos de guerra donde la incidencia de la obesidad y de la diabetes mellitus disminuye con la carencia de alimentos y con el tipo de dieta. Múltiples son los estudios estadísticos que correlacionan ambas condiciones. Sin embargo, la obesidad no es el único factor y no



está presente en todos los diabéticos. Al parecer, por lo menos en los juveniles, la enfermedad predomina en ciertas épocas del año, correlacionándola algunos autores con enfermedades virales, destacando los virus Coxachie B, de la parotiditis, de la mononucleosis infecciosa y el del sarampión alemán. Diversos virus (Fig. 8) afectan el páncreas, variando éstos en las distintas especies.

La etiología viral y la genética no se excluyen una de la otra. Receptores celulares a agentes infecciosos podrían determinar quien se afectaría por ellos. Dichos receptores han sido demostrados en varias condiciones infecciosas, transmitiéndose de forma hereditaria (18). Si los genes determinan el que estos agentes infectan, ¿cómo llamaremos entonces a la enfermedad en sí? ¿Se tratará de una condición hereditaria o de una condición infecciosa?

Se ha propuesto que en la diabetes, se hereda el receptor para el virus betatrópico (19). Podría ser que en la diabetes lo que exista es un trastorno en la regeneración de la masa de células beta pancreáticas. Si los islotes son afectados por un virus en una persona normal y la destrucción no es total, podría ocurrir una regeneración total, mientras que en un sujeto predispuesto a la diabetes, la destrucción sería irreversible, dando lugar a una deprivación de insulina.

Otra probabilidad es que los virus inicien o desencadenen un mecanismo autoinmune. El virus podría ejercer un efecto directo en la célula beta dando lugar a daño celular que servirían de antígenos por sí solos o en conjunto con el virus, induciendo la producción de anticuerpos. Los trabajos de Nerup y colaboradores (20) sugieren esto, y diversos autores (21-24) han confirmado la presencia de anticuerpos antipancréaticos no antiinsulínicos en diabéticos nuevos.

En los últimos años se han podido establecer diferencias fenotípicas entre los diabéticos insulíno-dependientes, inestables, y los diabéticos estables. Estudios genéticos tienden a demostrar que son enfermedades diferentes.

Se ha observado una asociación con enfermedades de tipo autoinmune, al igual que la pre-

Virus que afectan el páncreas modificado de Steinke, J. y Taylor, K. W. <sup>17</sup>		
Virus	Sujeto	Autor
Paperas	hombre	Kremer 1947 Hinden 1962 Mc Crole 1963
Coxackie B	ratón	Pappen Burch 1971
	hombre	Kibrick 1956
Reovirus	ratón	Stanley y colabs. 1953
Necrosis pan-creatica infecciosa	trucha	Wood y colabs. 1965
Pié - boca	ganado	Pedini y colabs. 1962
Mononucleosis infecciosa	hombre	Wislockie 1966
Encefalomio-carditis	ratón marmota	Craighead y colabs. 1966, 1971, 1972
Rubella	hombre	Forrest y colabs. 1969, 1971

Figura 8

sencia de anticuerpos antipancréaticos y contra otros tejidos en los diabéticos juveniles. Ello tiende a implicar procesos autoinmunes en su patogenia. Lendium y colabs. (24) han observado una frecuencia de anticuerpos antipancréaticos en el 38 por ciento de los juveniles, en 5 por ciento de los estables, y en 1.7 por ciento de sujetos no diabéticos. En el grupo de inestables, los anticuerpos antipancréaticos fueron hallados en el 85 por ciento de los sujetos inmediatamente después del comienzo de los síntomas, disminuyendo según progresó la condición. Se trata de anticuerpos anticitoplasmáticos y no antiinsulínicos que probablemente aparecen después del daño celular y antes de la aparición de síntomas.

Nosotros (25) hemos observado una relación entre el síndrome de sarampión alemán congénito y la tiroiditis crónica, enfermedad de tipo autoinmune. Previamente la condición también había sido asociada a diabetes mellitus. La asociación con tiroiditis crónica ha sido confirmada poste-

riormente por otros autores norteamericanos e ingleses. Nuestra paciente recientemente desarrolló diabetes mellitus insulín dependiente, lo que tiende a implicar más aún este virus en la etiopatogenia de diabetes y fortalece la hipótesis de daño celular y mecanismos autoinmunes. Es sabido que en los pacientes con síndrome de sarampión alemán congénito y diabetes mellitus hay una mayor incidencia de HLA B8 (31).

El pasado año, en un simposio de la Asociación Americana de Diabetes en Norteamérica, se informó que la estreptotocina a dosis pequeñas da lugar a cambios inflamatorios mínimos en las células Beta de animales de experimentación. Inicialmente ocurre una inflamación localizada en los islotes, llenándose posteriormente las células Beta de unas partículas virales (tipo C). Las células mueren en un período de 2-3 semanas instaurándose un cuadro insulino-dependiente en los animales estudiados (33).

En los diabéticos juveniles, inestables, se ha observado una mayor incidencia de los antígenos HLA B8, W15 y del locus D, los cuales podrían estar asociados o relacionados con el gen o genes diabetogénicos (26-28). Entre las diversas condiciones autoinmunes que se asocian con diabetes se observa también una mayor incidencia de estos antígenos.

La época del año en que aparece la condición en niños HLA 8 positivos difiere de los que no presentan este antígeno, según lo demuestran los datos de Roller y colaboradores (29) (Fig. 10). Se observa que en los niños HLA 8 positivos hay una variación estacionaria a diferencia de los no positivos. Se observa además, que las infecciones virales por virus Coxackie B ocurren 2-3 meses antes de la presentación de la condición en los HLA 8 positivos. Ello tenderá a confirmar la hipótesis de origen viral. Se sabe que sujetos con HLA 8 o W-15 positivos tienen un riesgo 2-3 veces mayor de adquirir diabetes mellitus inestable. Con probabilidad el HLA-8 puede estar asociado con un virus y el W-15 con otro (30). En los sujetos afectados del síndrome de sarampión y diabetes mellitus hay un aumento de incidencia

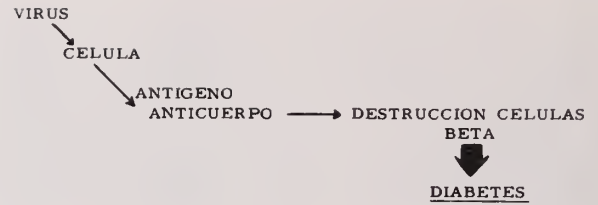


Figura 9

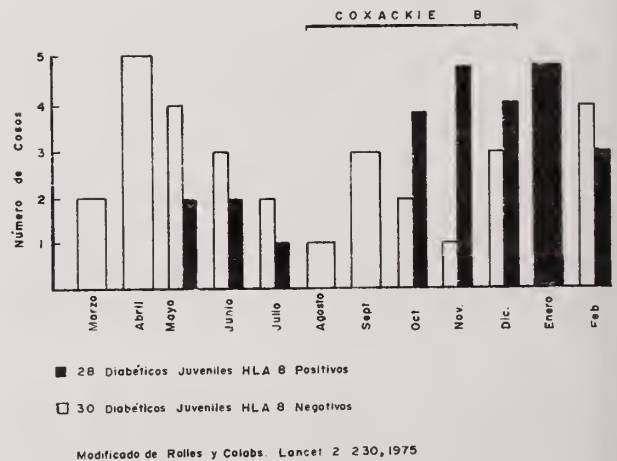


Figura 10

de HLA-8 pero no de W-15 (31). Poblaciones donde hay baja incidencia de HLA-8, concordantes, también tienen baja incidencia de diabetes mellitus.

En el caso de gemelos concordantes se ha observado un aumento en HLA-8 y en los discordantes de HL W15, lo que sugiere que aún en los discordantes hay predisposición genética, la que probablemente viene determinada por alelos diferentes (32).

Los fenotipos de histocompatibilidad HLA vienen determinados por diversos locus en las regiones B, C, y D del cromosoma 6, donde probablemente residen el gen o genes diabetogénicos. Estos genes serían responsables de la susceptibilidad a la condición. Cualquier noxa daría lugar a cambios y daño a las células beta en los susceptibles (receptores para la infección), dando lugar a procesos de autoinmunidad que ayudarían a destruir las células beta.

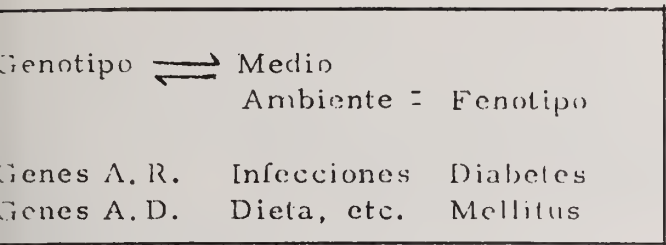


Figura 11

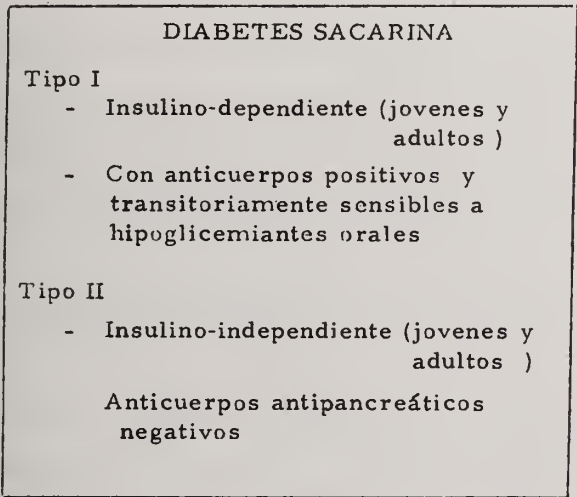


Figura 12

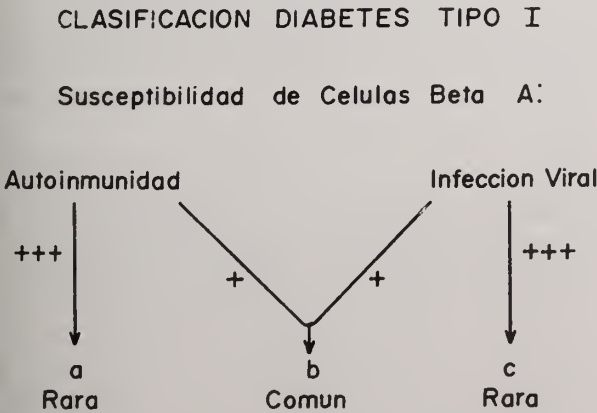


Figura 13

El genotipo del individuo dispondría del tipo de herencia, el cual al interaccionar con el medio ambiente, llevaría a los así susceptibles al cuadro fenotípico de diabetes manifiesta (Fig. 11).

Irvine (34), en Inglaterra, clasificó recientemente a los diabéticos según su insulino dependencia o independencia y la positividad o negatividad de anticuerpos antipancréaticos. Los diabéticos del tipo I (Fig. 12) corresponderían a los diabéticos inestables, en los cuales estarán presentes en su comienzo anticuerpos antipancréaticos, observándose tanto en niños como adultos. En este grupo se incluyen también sujetos con anticuerpos positivos, pero que responden transitoriamente a los hipoglicemiantes orales. Los subclasifica este autor en tres subgrupos, como se observa en la Figura 13, haciendo uso de los posibles factores etiopatogénicos de tipo autoinmune e infeccioso. Según observamos en la figura 13, los diversos subtipos dependerán de la interacción de estos factores.

En el tipo II incluye a los insulino-independientes, tanto adultos como jóvenes, con anticuerpos antipancréaticos negativos, correspondiendo a los diabéticos estables.

Las diferencias existentes entre la diabetes inestable y la estable, sugieren que se trata de entidades de origen diferente que dan lugar a un defecto metabólico similar. En la primera, tendría más importancia el factor exógeno (¿infeccioso?) que el hereditario, mostrándose una vez más la interrelación entre el medio ambiente y la herencia en la manifestación de diversas condiciones. Es indiscutible que en la epidemiología de la diabetes intervienen tanto factores hereditarios como ambientales. Nos encontramos en el umbral de determinar estos caracteres observando como interaccionan ambos factores causales. La detección de nuevos marcadores genéticos, nos dará más luz sobre la condición.

Basados en lo anteriormente expuesto y a nuestra experiencia respaldamos la hipótesis unitaria de predisposición genética para todos los tipos de diabetes, con heterogeneidad en las formas de herencia, y un factor infeccioso y





autoinmune de extraordinaria importancia en los diabéticos insulino-dependientes.

### Agradecimiento

Agradecemos a los Dres. C. Salinas de Carolina del Sur, Dr. J. García Castro de P. R. y al Dr. B. Nusinovich de Argentina la lectura crítica y comentarios sobre el manuscrito, al igual que a la Sra. Rosa J. Munier y la Sra. Mirna Nazario por la labor clerical.

### Referencias

1. Marble, A., White, P., Bradley, R. F., Krall, L. P. (editores): Joslin's Diabetes Mellitus-Filadelfia, Lea & Febiger, 11a edición, 1973, Pag. 3.
2. Pincus, G., y White, P.: On the inheritance of diabetes mellitus. I. An Analysis of 675 family histories. Amer. J. Med. Sci. 186, 1, 1933.
3. Rosenthal, M. B. y Goldfine, I. D.: Inheritance of Diabetes Mellitus. N. England J. Med. 295: 1321, 1976.
4. Cammidge, P. J.: Diabetes Mellitus and heredity. Brit. Med. J. 2: 738, 1928.
5. Cammidge, P. J.: Heredity as a factor in the aetiology of diabetes mellitus. Lancet 1: 393, 1934.
6. Harris, H.: The familial distribution of diabetes mellitus; a study of the relatives of 1241 diabetic propositi. Ann. Eugen. 15: 95, 1950.
7. Lamy, M., Frezal, Jr., y Grouchy, J. de: Résultats d'une enquête sur l'hérédité du diabète sucré. Rev. Franc. Etud. Clin. Biol. 2: 907, 1957.
8. Stimmler, L., y Elliot, R. B.: Inheritance of diabetic serum factor inhibiting normal utilization of insulin. Lancet 1: 956, 1964.
9. Steinberg, A. S.: Genetics and diabetes. On the nature and treatment of diabetes. Proc. 5th Congress Int. Diabetes Federation. Excerpta Medica Foundation, 1965, pg. 601.
10. Simpson, N. E.: Multifactorial inheritance, a possible hypothesis for diabetes. Diabetes 13: 462, 1964.
11. Neel, J. V., Fajans, S. S., Conn, J. W. y Davidson, R. J.: The evaluation of genetic factors in selected illustrative diseases.

- Diabetes Mellitus. U. S. Public Health Service Pub. No. 1163, 105, 1965.
12. Bennett, P. H., Rushforth, N. B., Steinberg, A. G., Burch, T. A., y Miller, M.: Diabetes in the Pima Indians: evidence of bimodality in glucose tolerance distributions. Diabetes. 18: 333, 1969.
13. Renold, A. E., Stauffacher, W. y colabs.: En "The Metabolic Basis of Inherited disease. 3ra. edición, Stanbury, J. B., Wyngaarden, J. B. y Frederickson, D. S. (editores), Nueva York, Mc Graw-Hill Book Co. 1972, pg. 83-118.
14. Bennett, P. H., Burch, T. A. y colabs. Lancet 2: 125, 1971.
15. Neel, J. V.: En "Early Diabetes", Camerini-Davalos, R. y Cole, H. S. (editores), Nueva York, Academic Press, 1970, pg. 3-10.
16. Marble, A., White, P., Bradley, R. F., Krall, L. P. (editores) Joslin's Diabetes Mellitus. Filadelfia. Lea & Febiger 11a edición, 1973, pg. 23.
17. Steinke, J. y Taylor, K. W.: Viruses and the etiology of Diabetes. Diabetes 23: 631, 1974.
18. Gerald, P. S.: A new frontier for infectious disease research. N. Engl. J. Med. 295: 337, 1976.
19. Levy, N. L. y Notkins, A. L.: Viral infections and diseases of the endocrine system. J. Infect. Dis. 124: 94, 1971.
20. Nerup, J., Anderson, O. O., Bendixen, G., Egeberg, J., y Poulsen, J. E.: Antipancreatic cellular hypersensitivity in diabetes mellitus. Diabetes 20: 424, 1971.
21. Irvine, W. J., Gray, R. S., McCallum, C. J.: Pancreatic islet cell antibody as a marker for asymptomatic and latent diabetes and prediabetes. Lancet 2: 1097, 1976.
22. Bottazzo, G. F., Florin-Christensen, A. y Domach, D.: Islet-cell antibodies in Diabetes Mellitus with autoimmune polyendocrine deficiencies. Lancet 2: 1279, 1976.
23. Lendium, R., Walker, G. y Gamble, D. R.: Islet-cell antibodies in juvenile diabetes mellitus of recent onset. Lancet 1: 880, 1975.
24. Lendium, R., Walker, G., Cudworth, A. G. y colabs.: Islet-cell antibodies in diabetes mellitus. Lancet 2: 1273, 1976.
25. Pérez Comas, A.: Congenital Rubella and acquired hypothyroidism secondary to Hashimoto's thyroiditis. J. of Pediat. 88: 1065, 1976.
26. Nerup, J., Platz, P., Ortvad-Andersen, Christy, M., y colabs.: HL-A antigens and Diabetes Mellitus. Lancet 2: 864, 1974.
27. Cudworth, A. G. y Woodrow, J. C.: Evidence for HL-A Linked Genes in "juvenile" diabetes mellitus. Brit. Med. J. 3: 133, 1975.
28. Cudworth, A. G. y Woodrow, J. C.: HL-A antigens and diabetes mellitus. Lancet 2: 1153, 1974.
29. Rolles, C. J., Rayner, P. H. W., y Mackintosh, P.: Actiology of Juvenile diabetes. Lancet 2: 230, 1975.
30. Cudworth, A. G., Woodrow, J. C., Gamble, D. R.: Coxsackie B<sub>4</sub> Virus infection and diabetes. Lancet 2: 29, 1975.
31. Menser, M. A., Forrest, J. M., Honeyman, M. C.: Rubella Syndrome and diabetes Mellitus. Lancet 2: 1509, 1974.
32. Nelson, P. G., Pyke, D. A., Cudworth, A. G., Woodrow, J. C. y Batchelas, J. R.: Histocompatibility antigens in diabetic identical twins. Lancet 2: 193, 1975.
33. Fells, P. W.: Diabetes Progress 1976. Advancing attack against Diabetes. Diabetes Forecast 30: 4, 1976.
34. Irvine, W. J.: Classification of Idiopathic diabetes. Lancet 1: 638, 1977.

# CARDIAC PACEMAKER THERAPY DURING PREGNANCY, LABOR AND DELIVERY FOR HEART BLOCK

Charles D. Johnson, MD

**Summary:** This communication documents a young female with heart block in whom a permanent epicardial demand pacemaker had previously been placed. Her pregnancy, labor and delivery were uneventful. A review of the small number of other such reported cases was made. Pacemaker therapy in these patients has been in general quite rewarding and without morbidity or mortality.

**Resumen:** Este trabajo presenta el caso de una paciente joven con historial de bloqueo completo del corazón, a la cual se había previamente implantado un marcapaso epicárdico permanente, del tipo de demanda. Esta paciente toleró sin problema alguno, su embarazo, parto y alumbramiento. En el trabajo se hace una revisión de los otros casos similares reportados en la literatura médica. El tratamiento de estos casos utilizando marcapasos ha sido exitoso sin problemas significativos de morbilidad o mortalidad.

Pregnancy may be associated with cardiac arrhythmias and may occur in the course of patients with arrhythmias and heart block (1-4).

Pregnancy has infrequently culminated in patients with complete or high-grade atrioventricular (AV) heart block, demanding additional therapeutic and management considerations, which may comprise an artificial cardiac pacemaker during labor and delivery. A patient who had a previous permanent pacemaker for heart block (HB) in whom pregnancy ensued, and who presented a therapeutic dilemma, is reported.

## Case Report

This 21-year old female, Gr 1, P 0, Ab O, was first seen at the University Hospital, Centro Médico, at the age of 14 years. Chest pain, palpitations, dyspnea and dizziness were early symptoms. Cardiac catheterization did not sustain the clinical impression of a possible atrial septal defect. Heart rates in the 40's and 50's were present, with a slight increase in rate on exercise. Black-out spells and brief loss of consciousness were suffered. Electrocardiograms (ECG) over the years have revealed right axis deviation, complete right bundle branch block (RBBB), followed by 2:1 second degree, high-grade and complete HB, ventricular capture beats, concealed and supernormal conduction, and perhaps idiojunctional rhythm with bifascicular block, or less likely a trifascicular block (unfortunately, a His Bundle recording was not available) (Figure 1). The etiology of her heart block is not known; viral myocarditis was considered, but a congenital block has been regarded more likely. Medical therapy consisting of sublingual isoproterenol, probanthine, ephedrine and observation was tried initially. However, later, at age 16 years (1972)



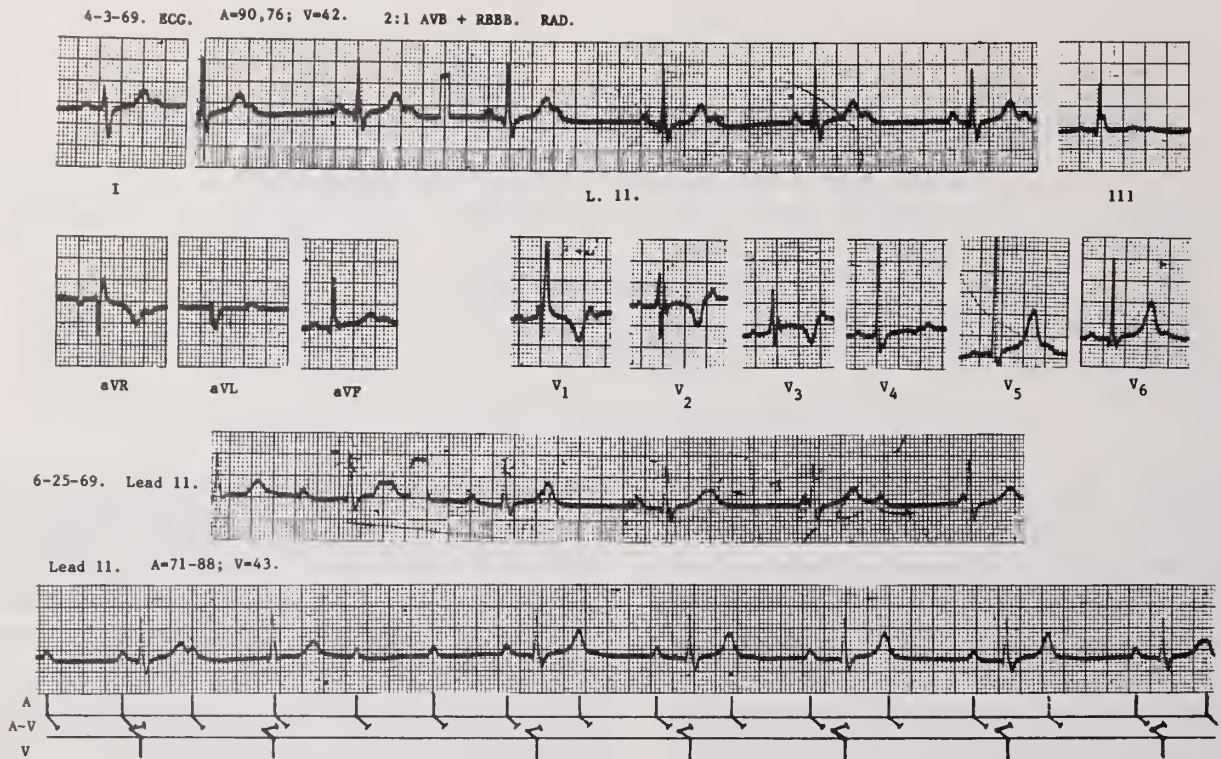


Figure 1: 14-year old female. AV block, probably congenital. Right axis deviation. 2:1, high-grade and complete AV block. AV dissociation. Probably idio-ventricular rhythm with bifascicular block — right bundle branch block and left posterior hemiblock. Capture beats. Concealed and supernormal conduction.

she remained symptomatic, with a heart rate of 48 per minute or less, with high-grade and complete AV block (lower focus with a RBBB pattern similar to that when patient was conducting 1:1 and 2:1 from the sinoatrial node). After a prior temporary pacemaker, on 2-9-72, a Medtronic permanent, left ventricular (LV), epicardial demand pacemaker was placed at a rate of 70 per minute, with the generator beneath the pectoral muscle and left breast. A post-pericardiotomy syndrome with mild right heart failure occurred subsequently and then resided. The patient has done well over the subsequent years. On 8-19-74, a new Medtronic generator (Model 5945, voltage 5.06 and current 10.12 ma) was placed, at a rate of 71. The patient got married and became pregnant. ECG's showed a pacemaker rhythm with complete ventricular capture and rates of 67-68 per minute (Figure 2). She has been asymptomatic. The patient was followed more closely near term. Her ex-

pected date of confinement (EDC) was 10-17-76 (40 weeks gestation). Studies on the pacemaker by Medtronic revealed a pacing interval of 890 msec (rate of about 67), a pulse width of 54 msec (4 msec wider) and normal sensing. The projected life of the pacemaker is 4 years.

She was admitted prior to the EDC for closer observation and decision on management. An induction trial on 10-15-76 for 6 hours using oxytocin injection and ECG monitoring was attempted, without success. The placement of a second temporary cardiac pacemaker for labor and delivery as originally recommended, was later decided against. The blood pressure was 100/80 and one pulse rate was recorded as 100. Labor occurred after amionotomy was performed. Fetal monitoring revealed a rate of 140-150 per minute; the patient's pulse rates were 68-70 and the blood pressure remained normal. Under pudendal block and with oxy-



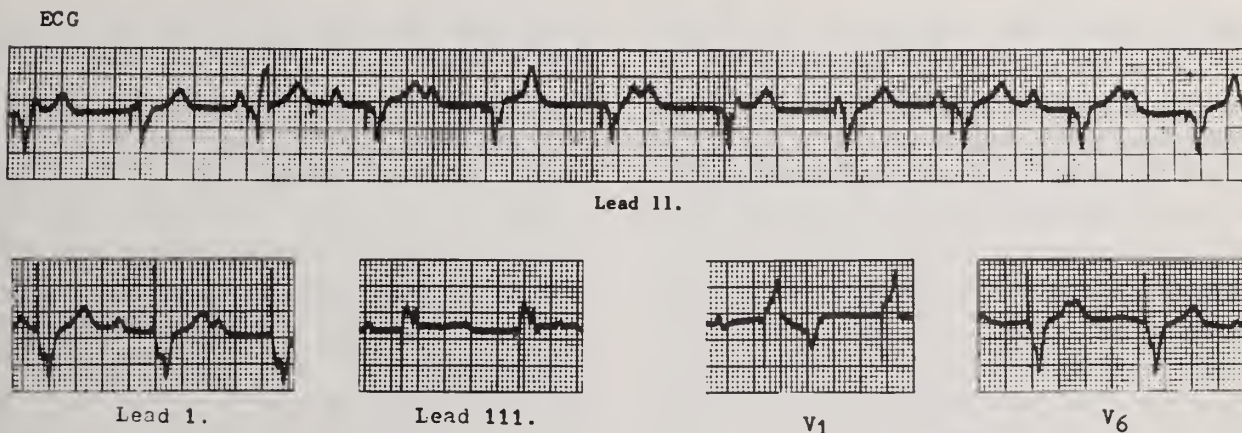


Figure 2: 8-27-76. Age 21 years. ECG — Epicardial demand pacemaker.

tocin injection, meperidine and diazepam, delivery of a normal baby (vertex, APGAR score 8-9) ensued, early on 10-17-76. A third degree perineal tear was suffered; total length of labor was 6 hours and 52 minutes (1st stage— 6 hours and 20 minutes, 2nd stage— 30 minutes, 3rd stage— 2 minutes). The postpartum pacemaker rate was 68 and the patient's subsequent course uncomplicated. The ECG was unchanged from that of Figure 2.

### Discussion

Cardiac conduction defects are seen infrequently in the course of pregnancy Nanta (5), in 1914, reported the first case of acquired complete HB, and Laubry (6), in 1927, the first case of congenital complete HB in pregnancy. Complete and high-grade AV conduction defects are quite unusual, and may be of acquired or congenital etiology. Such defects often have created no special obstetrical problems and delivery has been uncomplicated. Symptoms range from giddiness and faintness to asymptomatic bradycardia. However, rarely cardiac and maternal complications have been experienced, even including Stokes-Adams attacks and maternal deaths (1-4, 7, 8).

### *Review of the previously reported cases.*

By 1951, a total of 45 cases of HB and pregnancy were found from the world's literature, with a total of 6 maternal deaths, 4 of which were related directly to the association of the block and pregnancy (1). Electronic cardiac pacing was not employed in any of these cases. In 1956, Mendelson (2) reviewed 47 cases, 26 acquired and 21 of congenital origin (half of whom had an associated ventricular septal defect). There was 1 case with sinoatrial block. Heart failure occurred in 6 percent, toxemia in 9 percent, maternal deaths in 13 percent and fetal deaths in 15 percent of the cases, although the majority of pregnancies and deliveries went uncomplicated. Gravidity was 1-3 and ages ranged from 22-36 years. The outlook for the mother and fetus depends upon the associated lesions more than the heart block. Slowing or sudden failure of idioventricular rhythm may result in syncope, convulsions or death. Complications are less if the block is congenital, if the QRS width is normal and if the heart rate augments with exercise (2-4). By 1966, there were 75 case reports of congenital and acquired complete HB associated with

pregnancy (9).

Pacemaker therapy during pregnancy was first reported by Shouse & Acker in 1964 (10). A Medtronic bipolar LV pacemaker (rate 70, 8-10 ma) was placed before pregnancy in a 26-year old female with 2:1 and 3:1 AV block with a heart rate of 40-50, who previously suffered syncope, Stokes-Adams seizures, ventricular flutter and fibrillation. The prenatal course was uneventful. Eight hours post-partum there was a sudden increase in heart rate with an irregular rhythm, believed due to the stress of delivery. The pacemaker voltage was increased to 15 ma and the rate to 85; the heart resumed regular response, and over the next 48 hours the voltage was gradually returned to 10 ma. During the second stage low forceps were used; anesthesia comprised cyclopropane and oxygen. Labor, delivery, puerparium, patient and the infant were normal. The authors concluded that similar patients should not be discouraged to get pregnant.

A few other such cases have been documented: Buchner (11); Schonbaum (9) — a patient in whom a previous labor was almost catastrophic, experienced no difficulty in labor during which a transvenous pacemaker was employed for a few hours. A temporary transvenous pacemaker served well during labor and delivery in a 40-year old female who had sustained an acute anterior myocardial infarction and complete HB 5 years prior (12). It was inserted 3 days prior to labor and delivery when the patient's pulse was 48. She was paced at 60 per minute, later augmented to 80. The pacemaker was chosen to augment the patient's ability to withstand the stress of anesthesia, labor and delivery. It was mentioned that during heart block sudden slowing or failure of the ventricular pacemaker from hypoxia, acidosis, excessive vagal stimulation or anesthetic agents could induce dizziness, syncope, convulsions or death. A temporary right ventricular (RV) pacemaker, under ECG monitoring, was exploited in a 24-year old woman with congenital complete HB and an idiojunctional rhythm.

The pacing rate was increased from 72 to 85. Saddle block, low forceps and oxytocin induction were used. The rate was gradually reduced over the next 24 hours, and the pacemaker was then removed (13). A 21-year old female, Gr 1, P O, with Ebstein's Anomaly and sinus bradycardia-junctional tachycardia syndrome, was managed successfully with a temporary Medtronic, bipolar pacemaker during labor and delivery, after multiple anti-arrhythmic drugs had failed. Pacing at 98 per minute was adequate to overdrive the tachycardia. The pacemaker was removed 2 days after an uneventful delivery (14).

In conclusion, approximately 14 cases of pacemaker therapy during pregnancy have been reported, all without maternal or fetal mortality. Various methods of pacemaker application have served: intravenous, epicardial, temporary pacing and permanent units in place prior to pregnancy. Complete AV block, either congenital or acquired, has been the major indication for pacing. Morbidity and complications have been minimal, comprising temporary loss of capture requiring an increase in milliamperage (10), transient pacemaker competition (11), and rarely generator failure— not related to the pregnancy and probably not to the location of the generator either. Buchner (11) noted 2 instances of such in which the unit was located in the left rectus sheath. However, battery complications were not observed in a 23-year old female who had the demand generator implanted in the subcutaneous tissues of the abdominal wall throughout pregnancy, for congenital 2:1 and complete AV block, ventricular tachycardia and junctional rhythm. Tension of the skin over the generator site was no problem, and the incision healed well after the generator was replaced for anticipated failure a few days prior to delivery. Cesarean section produced a normal baby (15). And finally, concern has been expressed that a pacemaker battery located in the breast region during pregnancy could result in irritation and ulceration, aggravated by



the increased breast size. Such has occurred but without consequences (16). A 29-year old patient with cardiomyopathy, congenital complete HB and Adams-Stokes attacks, with a ventricular rate of 50, had a Devices permanent, endocardial RV, fixed-rate pacemaker inserted via the left external jugular vein (rate 70/min), with the generator implanted subcutaneously in the left supramammary region. Three months later she became pregnant. At the 16th week of pregnancy the generator was reimplanted deep to the pectoral muscles because of skin ulceration. Premature labor occurred at 30 weeks. The heart rate remained constant and the pacemaker functioned normally (17). The authors noted that with a fixed-rate unit there is no rise in heart rate as normally occurs in pregnancy, and that the cardiac output is raised only by an augmented stroke volume. This is achieved successfully in most cases, as shown by the relative rarity of congestive heart failure (their review uncovered only 3 cases: 1 associated with toxemia and 2 due to underlying myocardial disease). They stated that dyspnea and peripheral edema may occur to a greater degree than in normal pregnancy, but that this does not necessitate in-hospital therapy. They also believed that pregnancy in such patients was not contra-indicated, other than for a previous history of heart failure, as pacemaker therapy may be utilized providing there is no severe myocardial disease. One case with the box in the left rectus sheath noted pain at the 4th month of gestation. All these had permanent units installed prior to becoming pregnant.

It is stated that patients with no history of previous Stokes-Adams attacks can be managed expectantly with drugs and a pacemaker at the bedside, but that those women who have suffered such attacks during pregnancy are best managed by insertion of a temporary transvenous pacemaker (4). Such an approach allows control of rhythm and conduction

disturbances complicating pregnancy; an adequate rate may be maintained avoiding bradycardia, an augmented stroke volume and the deleterious effects of drugs on the mother and depression of fetal heart contractility and rate. Pacemaker therapy has proven to be safe and reliable, and has offered no special difficulties with pregnancy, labor and delivery (17).

There is no indication to interrupt gestation solely on the basis of heart block, and there are no indications for cesarean section in women with heart block, except for obstetrical ones.

There is a history of symptoms and Stokes-Adams attack in the patient reported, but she suffered none of these during pregnancy. Although a second temporary catheter placement was eventually decided against, an additional intravenous temporary catheter may be indicated in such patients to augment the mother's heart rate to a more physiological one during the added stress and cardiac work of labor and delivery. No noninvasive means was available to increase the rate of the pacemaker unit.

## References

1. Epstein, J. R., Altman, H. E.: Heart block in pregnancy. *Med Ann DC* 20: 660-663, 1951.
2. Mendelson, C. L.: Disorders of the heartbeat during pregnancy. *Am J Obstet Gynec* 72: 1268-1301, 1956.
3. Kaufman, J. M., Ruble, P. E.: The current status of the pregnant cardiac. *Ann Intern Med* 48: 1157-1170, 1958.
4. Bemiller, C. R., Forker, A. D., Morgan, J. R.: Complete heart block, prosthetic aortic valve, and successful pregnancy. *JAMA* 214: 915, 1970.
5. Nanta, A.: Heart block in pregnancy. *Arch Mal Coeur* 7: 305-308, 1914.
6. Laubry, C.: Complete heart block in pregnancy. *Bull Soc Med Hop Paris* 51: 126-127, 1927.
7. Veray, F. X.: Personal communication, 1976.
8. Kenmure, A. C. F., Cameron, A. J. V.: Congenital complete heart block in pregnancy. *Br Heart J* 29: 910-912, 1967.
9. Schonbaum, M., Rowland, W., Quiroz, A. C.: Complete heart block in pregnancy. *Obstet Gynec* 27: 243-246, 1966.
10. Shouse, E. E., Acker, J. E.: Pregnancy and delivery in a patient with external-internal cardiac pacemaker. *Obstet & Gynec.* 24: 817-818, 1964.



11. Buchner, V. C., Bilger, R., Overbeck, W., et al: Geburt bei einer Patientin mit künstlichem Schrittmacher des Herzens. *Deutsch Med Wschr* 89: 1932-1933, 1964.
12. Guiffrida, J. C., Bizzarri, D. V., Lagman, W., et al: Obstetrical anesthesia in myocardial infarction and complete heart block. *JAMA* 204: 617-620, 1968.
13. Gusdon, J. P., Spencer, W. J.: The use of an internal pacemaker during labor in a patient with heart block. *South Med J* 65: 112-113, 1972.
14. Schatz, J. W., Fischer, J. A., Lee, F., et al: Pacemaker therapy in pregnancy for the management of sinus bradycardia-junctional tachycardia syndrome. *Chest* 65: 461-463, 1974.
15. Middleton, E. B., Lee, Y. C.: Pregnancy associated with cardiac pacemaker generator implanted in abdominal wall. A case report. *Obstet & Gynec* 38: 272-275, 1971.
16. Berestka, S. A., Spellacy, W. N.: Complete heart block associated with pregnancy and treated with an internal pacemaker. *J Lancet* 87: 461-463, 1972.
17. Gins, H. M., Hollinrake, K.: Complete heart block in pregnancy treated with an internal pacemaker. *J Obstet Gynaec Brit Comm* 77: 719-722, 1970.
18. Todisco, T.: Complete atrioventricular block in pregnancy (Resuscitation and treatment with intracardiac pacemaker during labor). *Boll Soc Ital Cardiol* 17: 1243-1250, 1972.
19. Diakowska-Ostaszewska, M.: Complete atrioventricular block in a pregnant woman treated with prophylactic cardiac pacing during cesarean section. *Wiad Lek* 29: 1165-1167, 1976.

# THE CAT-CRY SYNDROME, AN UNUSUAL CHROMOSOMAL ABERRATION: REPORT OF A CASE AND REVIEW OF THE LITERATURE

Fermín Sánchez-Lugo, MD, José M. García-Castro, MD and Luz Carlota Reyes de Torres, MS

**Summary:** A case of the "cri-du-chat" syndrome, 46, XX, del (5) (qter→p12:), born in Puerto Rico is presented. A description of the clinical and chromosomal findings are given, as well as the desirability of genetic counseling and prenatal diagnosis in these cases.

**Resumen:** Se presenta un caso del síndrome del maullido del gato, 46, XX, del (5) (qter→p12:), nacido en Puerto Rico. Se detallan los hallazgos clínicos y cromosómicos y se apunta la deseabilidad del asesoramiento genético y del diagnóstico prenatal en estos casos.

Chromosomal abnormalities are a very common finding in the human species. It has been estimated that approximately one out of every two hundred liveborns exhibit some kind of chromosomal anomaly, many of which are of such a minor nature that do not produce clinical symptomatology, at least to the extent determined by our present knowledge. One of the objectives of the Regional Medical Pro-

gram of Hereditary Diseases is the diagnosis of such anomalies. Recently we have diagnosed a case of a rare chromosomal aberration: deletion of the short arms of a chromosome number 5, the so-called "cri-du-chat" or cat-cry syndrome. To our knowledge, this is the first case to be reported in Puerto Rico.

## Case Presentation

J. S. G. is a female infant, the product of a non-consanguineous mating between a 24 years old father and a 21 years old mother. Gestation was full-term and was complicated at 3 months gestation by an urinary tract infection, which was treated successfully with antibiotics, and at 5 months with hypertension. Premature contractions occurred at 7 months gestation, but were inhibited by alcohol therapy. On 1 November 1976 an emergency caesarean section was performed because of fetal distress. At birth the infant weighed 2633 gms and measured 53.3 cms. She was noted to have peculiar facies, microcephaly and a cat-like cry. She was then referred to us for genetic evaluation.

At 4 months of age, the infant weighed 4994 gms, measured 59.7 cms and had a head circumference of 37.3 cms. The distance between the inner canthi was 2.9 cms while that of the external was 6.6 cms, giving a ratio of inner/external of 0.44. Activity was normal for her age. She was found to have a round and somewhat asymmetric face with prominent forehead, thin eyebrows, epicanthal folds, antimongoloid slanting of the palpebral fissures and normal eyes. Other findings include a nevus flammeus on the forehead, a broad and depressed nasal bridge with a globular nasal tip and anteverted nares, an elongated philtrum measuring 0.9 cms, normal lips, but the pala-

---

*From the University Children's Hospital, Sections of Pediatric Endocrinology and of Medical Genetics, and the Regional Medical Program of Hereditary Diseases, School of Medicine, University of Puerto Rico, San Juan, Puerto Rico.*

*Supported in part by grant 1G04-RM-0000-CA-01 of the Regional Medical Program, National Institutes of Health, Bethesda, Maryland. Reprint address: Dr. José M. García-Castro, Programa Médico Regional de Enfermedades Hereditarias, G. P. O. Apartado 1764, San Juan, Puerto Rico, 00936.*

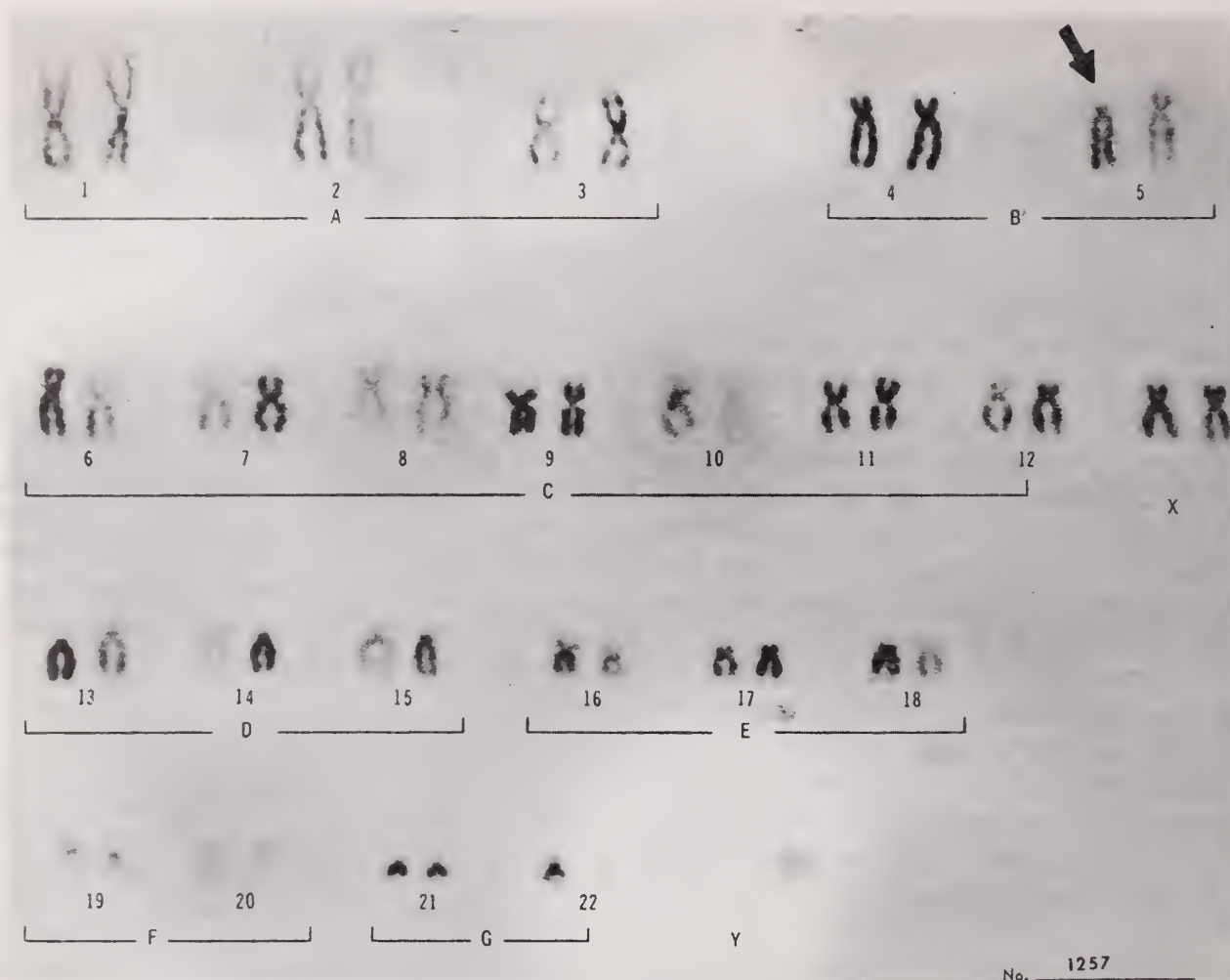


Figure 1: Karyotype of the present case. The arrow points to the deleted portion of one of the chromosomes number 5.

te was high-arched and there was micrognathia. The ears were low-set and with a slight posterior rotation. The pinnae were normal in configuration, but appeared to be large. Fingers and toes seemed particularly elongated. No other physical signs of importance were noted except for her cry which was weak, in spite of painful stimulation, and had a meowing, cat-like quality.

The family history revealed that the mother had had two previous abortions, both at 2 months gestation. The first was one of a twin pregnancy, and the second followed rubella vaccination in the mother. There was no pathological examination of these abor-

tuses. There have been no instances of children with similar findings as those present in our case in either side of the family.

Chromosome studies were performed and revealed a deletion of the short arms of one of the chromosomes number 5, identified through G-bands, in all of the metaphases analyzed. The deletion, however, did not include all of the short arm of the chromosome, but only the part distal to point p12. Her karyotype is, therefore, 46, XX, del (5) (qter→p12:) (See figure 1).



TABLE I  
Clinical Findings in the "Cri-du-chat" Syndrome

<i>Clinical Findings</i>	<i>Hamerton (8)</i>	<i>Smith (9)</i>	<i>Present Case</i>
<i>Failure to thrive</i>	<i>24 percent</i>	<i>100 percent</i>	<i>?</i>
<i>Mental retardation</i>	<i>100 percent</i>	<i>100 percent</i>	<i>?</i>
<i>Abnormal cry (cat-like)</i>	<i>87 percent</i>	<i>100 percent</i>	<i>+</i>
<i>Hypertelorism</i>	<i>73 percent</i>	<i>94 percent</i>	<i>+</i>
<i>Epicanthus</i>	<i>74 percent</i>	<i>85 percent</i>	<i>+</i>
<i>Microcephaly</i>	<i>95 percent</i>	<i>100 percent</i>	<i>+</i>
<i>Micrognathia</i>	<i>70 percent</i>	<i>N. D.</i>	<i>+</i>
<i>Oblique palpebral fissures (anti-mongoloid)</i>	<i>52 percent</i>	<i>81 percent</i>	<i>+</i>
<i>Abnormal ears</i>	<i>72 percent</i>	<i>58 percent</i>	<i>+</i>
<i>Hypotonia</i>	<i>61 percent</i>	<i>78 percent</i>	<i>-</i>
<i>Transverse palmar crease</i>	<i>18 percent</i>	<i>81 percent</i>	<i>-</i>
<i>Congenital Heart disease</i>	<i>71 percent</i>	<i>30 percent</i>	<i>-</i>
<i>Strabismus</i>	<i>83 percent</i>	<i>61 percent</i>	<i>-</i>
<i>Round ("Moon") facies</i>	<i>71 percent</i>	<i>68 percent</i>	<i>+</i>

+ = *Present* ; - = *Not present* ; N. D. = *Not determined*.

## Discussion

The "cri-du-chat" syndrome was first described by Lejeune et al in 1963 (1). At present there are about 50 cases of the syndrome reported in the literature (2, 3, 4). The salient features of this condition are presented in Table I, where they are compared with the findings in our patient. Some of these findings may be seen in Figure 2. It must be noted that the most important findings of this syndrome are also present in our patient. Microcephaly is ascertained by a head circumference far below the 3rd. percentile, as is hypertelorism, not only by the clinical appearance, but by a canthal ratio of 0.44, the normal for this age being 0.36 (5). Although failure-to-thrive cannot be stated to

be present in our patient, her weight was barely at the third percentile, while the height was at the 10th. Clearly this must be assessed in future visits, as well as the intellectual development, for at the time of the examination, mental retardation could not be stated to be present. It is interesting to theorize that the absence of some of these signs might be related to the fact that the chromosome deletion observed in this patient did not include all of the short arm of a number 5 chromosome, but only that beyond point p12, that is, about 80 percent of the short arm. The majority of cases of the cat-cry syndrome are sporadic, but in about 10 percent of the cases, one of the parents is a balanced translocation carrier (6), thus having a risk of about 1 in 5 of having another child with this condition. The parents of our case are being evaluated



Figure 2: Salient clinical findings of our patient include hypertelorism, anti-mongoloid slant of the palpebral fissures and micrognathia.

at present. Should one of them be found to be a carrier, prenatal diagnosis in future pregnancies would be advisable.

The sign which names this syndrome, the cat-cry, was definitely present in our case, as was mentioned. However, it must be stressed that this extremely important finding, the result of a narrow larynx and a flabby epiglottis is transitory (7). Thus it behooves the pediatrician who may witness such a sign in a neonate to refer the infant as soon as convenient for chromosome analysis for the final and definite diagnosis.

#### Acknowledgment

We wish to thank Dr. Silvio Vélez-Estrada for referring this patient to us.

#### References

1. Lejeune, J., Lafourcade, J., Berger, R., Vialatte, J., Boeswillwald, M., Seringe, P. and Turpin, R.: Trois cas de délétion partielle du bras court du chromosome 5. *C. R. Acad. Sci. (D) (Paris)* 257: 3098, 1963.
2. Berg, J. M., Welhanty, J. D. A., Faunch, J. A. and Ridler, M. A. C.: Partial deletion of short arm of chromosome of the 4 and 5 group (Denver) in an adult male. *J. Mental Defic. Res.* 9: 219, 1965.
3. Breg, W. R., et al: The "cri-du-chat" syndrome in adolescents and adults. *J. Pediat.* 77: 782, 1970.
4. Gordon, R. R. and Cooke, P.: Facial appearance in cri-du-chat syndrome. *Dev. Med. Child Neurol.* 10: 69-76, 1968.
5. Feingold, M. and Bossert, W. H.: *Birth Defects* Vol. 10 No. 13, 1974.
6. De Capoa, A., Warburton, D., Breg, W. R., Miller, D. A. and Miller, O. J.: Translocation heterozygosis: a cause of five cases of the "cri-du-chat" syndrome and two cases with a duplication of chromosomes number 5 in three families. *Am. J. Hum. Genet.* 19: 586-603, 1967.

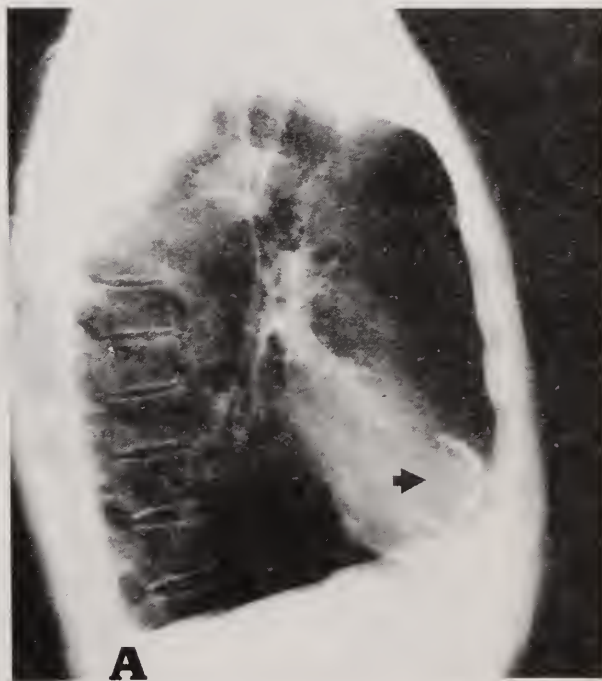
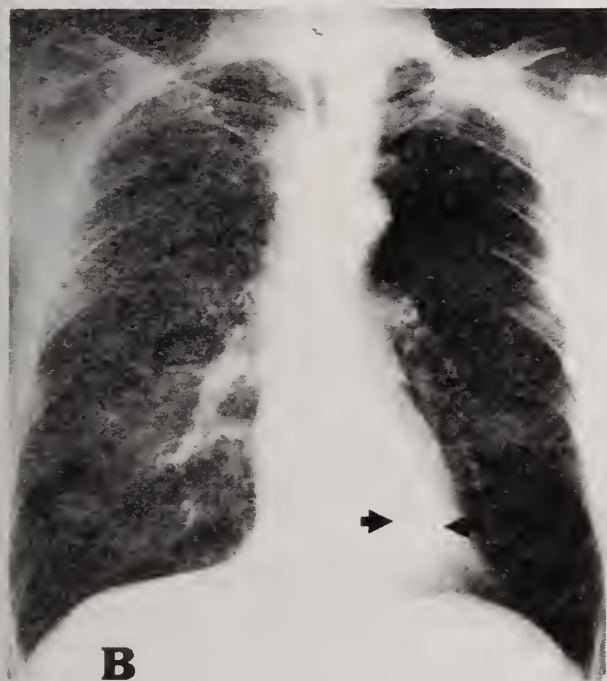
7. Ward, P. H., Engel, E. and Nace, W. E.: The larynx in the "cri-du-chat" (cat-cry) syndrome. Trans. Am. Acad. Ophthalmol. Otolaryngol. 72:90-102, 1968.
8. Hamerton, J. L.: Human cytogenetics Vol. II pp 354-356, Academic Press, New York, 1971.
9. Smith, D. W.: Recognizable patterns of human malformation, Second Edition, p 24, W. B. Saunders Co., Philadelphia, 1976.



A new section has recently been added to the Boletín. The purpose of this section is to illustrate significant electrocardiographic, angiographic, hemodynamic or radiologic findings in patients with or without cardiovascular diseases. Adequate illustrations will be accepted for publication provided that they comply with the regulations of the Boletín Asociación Médica de Puerto Rico. Each illustration should be sent in triplicate with an adequate interpretation and explanation of its clinical significance. All information should be sent to:

*GRAPHICS*  
*c/o Juan M. Aranda, MD*  
*Veterans Administration Hospital*  
*Box 4867 G. P. O.*  
*San Juan, Puerto Rico 00936*

The material will receive immediate consideration for publication. The authors will be informed within four weeks of the decision of the Editorial Board.



DIFFERENTIAL DIAGNOSIS:

1. Calcified Mitral Annulus
2. Calcified Ventricular Aneurysm
3. Pericardial Cyst
4. Lung Tumor



### *HISTORY:*

48 year old male with history of recurrent ventricular tachycardia and syncope. He presented for evaluation because of right sided hemiparesis. Physical examination revealed a sustained paradoxical apical impulse.

Radiographic evaluation revealed a normal size cardiac silhouette and extensive calcifications in the apex of the left ventricle (A, B. arrows). Angiographic studies revealed a calcified apical aneurysm with thrombus formation. The right sided hemiparesis was probably secondary to an arterial embolism. The cardiac shadow appears to be slightly enlarged three months after aneurysmectomy (C, D). The patient has been asymptomatic for ten months.

*Diagnosis:*

- Arteriosclerotic Heart Disease
- Antero-apical Infarction
- Apical Aneurysm
- Ventricular Tachycardia

*Juan M. Aranda, MD.*  
Chief, Cardiology Section  
Veterans Administration Hospital  
San Juan, Puerto Rico



## DIABETES MELLITUS: ¿HERENCIA O AMBIENTE?

*Como en tantos otros casos en medicina, la "solución" a una controversia entre la causa A y B de un fenómeno clínico, resulta ser la conciliación de A y B, en interacciones situacionales. Y cuando creemos que "sabemos" algo siempre hay un ¿por qué? ulterior.*

*En este número del Boletín (1) aparece un buen resumen de la controversia etiológica respecto a la diabetes mellitus: ¿herencia o ambiente? El consenso actual: probablemente ambos.*

*Sin duda, la mayor concordancia para diabetes entre gemelos idénticos, de hasta un 96 por ciento, en contraste con números mucho menores para gemelos dizigóticos (3 a 37 por ciento), da un buen argumento clínico al factor hereditario. Lástima que no haya aún parámetros confiables para buscar efectivamente, y caracterizar de una vez y por todas, la lesión o anomalía primaria del defecto bioquímico.*

*Las inconvenientes consecuencias de nuestros prejuicios respecto al patrón de herencia en diabetes han sido recientemente comentadas por Zonana y Rimoin (2), quienes señalan los riesgos de consejería genética equivocada y el mal uso que puede dársele al término "prediabetes", basados en una hipótesis de herencia autosómica recesiva, tomada como definitiva por algunos.*

*No menos importante es la consecuencia en actitud clínica de quienes, como Siperstein (3) aducen que la presencia de un aumento en el grosor de la membrana basal capilar en familiares de diabéticos previa la aparición de la hiperglicemia es indicio de que dicha complicación es inherente a la enfermedad, genéticamente determinada, y por, lo tanto, inútiles nuestros esfuerzos por ejercer un buen control bioquímico de la enfermedad para evitar las complicaciones vasculares a largo plazo.*

*De ahí que debamos estar receptivos a las más recientes informaciones, y que tengamos una mente amplia al respecto. Lo que hace varios años pareció un tanto superfluo respecto a la incidencia de anticuerpos antipancreáticos en diabéticos juveniles, ahora aparece como muy relevante a tenor con la creciente convicción de que dicho tipo de diabetes está asociada a insultos infecciosos, especialmente virales, y el rol que éstos puedan ejercer en el mecanismo de inmunidad del huésped.*

*Sin duda, que estamos bastante lejos de saber con certeza cómo y cuándo se origina la lesión pancreática. Más aún, todavía no está resuelto el rol que factores tales como el glucagon, la somatotropina, la somatomamotropina, el cortisol, la somatostatina, etc. puedan jugar en la etiología de la diabetes mellitus.*

*En tanto se esclarecen estas controversias etiopatológicas, cabe preguntar, como clínico práctico: ¿qué tiene el paciente que podamos tratar? La contestación: excesos dietéticos, obesidad...*

hiperglicemia. Sin duda, los recientes estudios experimentales en ratas y perros en los que pueden producirse lesiones típicas de microangiopatía induciendo la diabetes experimental, y su control al evitar la hiperglicemia, son altamente alentadores (4). En ausencia de un camino recto y seguro, tomemos la ruta del optimismo. Hagamos lo que esté en nuestras manos ahora: educación, control, y (así esperamos), prevención de complicaciones.

Francisco Aguiló, Jr., MD, FACP  
Director, División de Endocrinología  
y Metabolismo  
Hospital Universitario, Río Piedras, PR

### References

1. Pérez Comas, A.: Herencia vs. Ambiente en Diabetes Mellitus Bol. Asoc. Méd. P. Rico
2. Zonana, J. y Rimoin, D. L.: Current Concepts in Genetics. Inheritance of Diabetes Mellitus. New Engl. J. Med. 295: 603-605, 1976.
3. Siperstein, M. D., Unger, R. H., Madison, L. L.: Studies of muscle capillary basement membrane in normal subjects, diabetic and pre-diabetic patient. J. Clin. Invest. 47: 1973-99, 1968.
4. Bloodworth, J. M. B., Engerman, R. L.: Diabetic Microangiopathy in the Experimentally - Diabetic Dog and its Prevention by Careful Control with Insulin. Diabetes. 22: 290, (Suppl. 1) 1973.



## Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

**Most Widely Prescribed**—Antivert is the most widely prescribed agent for the management of vertigo\* associated with diseases affecting the vestibular system such as Menière's disease, labyrinthitis, and vestibular neuronitis.

**Relief of Nausea and Vomiting**—Antivert/25 can relieve the nausea and vomiting often associated with vertigo\*.

**Dosage for Vertigo\***—The usual adult dosage for Antivert/25 is one tablet t.i.d.

### BRIEF SUMMARY OF PRESCRIBING INFORMATION

**\*INDICATIONS** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

**Effective:** Management of nausea and vomiting and dizziness associated with motion sickness.

**Possibly Effective:** Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

**CONTRAINDICATIONS.** Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

**WARNINGS.** Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.


**Usage in Children:** Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

**Usage in Pregnancy:** See "Contraindications."

**ADVERSE REACTIONS.** Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

**ROERIG**   
A division of Pfizer Pharmaceuticals  
New York, New York 10017

**Antivert<sup>®</sup>/25**   
(meclizine HCl) 25 mg. Tablets  
**for vertigo\***



# GET MOVING, AMERICA!

It feels good to feel fit  
physically, mentally, emotionally  
So learn a skill you can play for life.



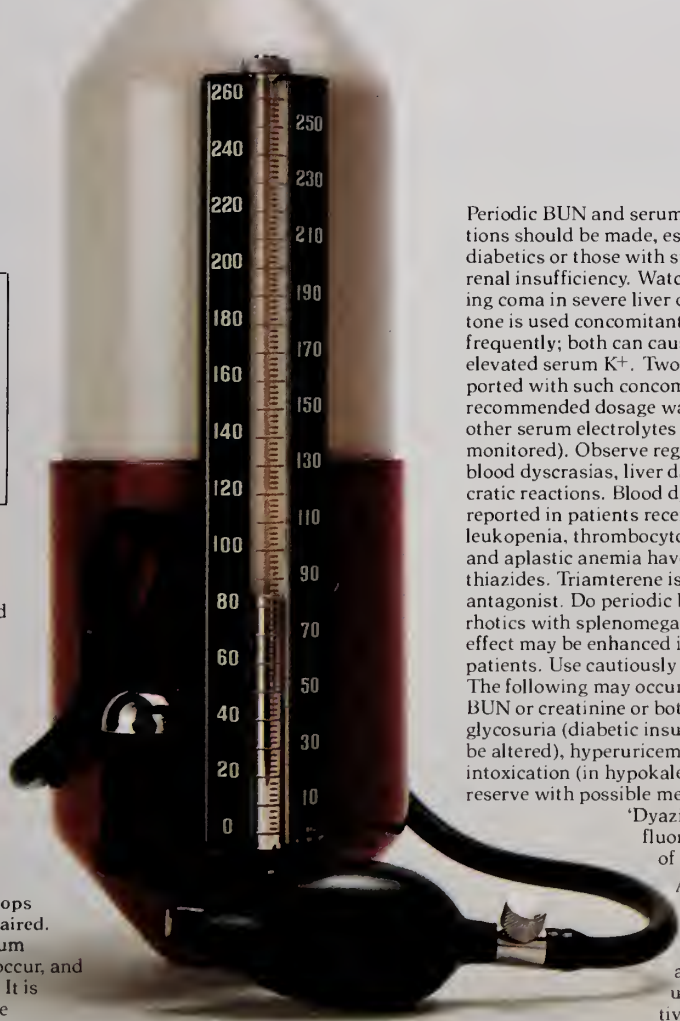
Sponsored by  
American Alliance for Health, Physical Education and Recreation  
1201-16th Street, N W , Washington, D C. 20036



# TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE **DYAZIDE®**

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE



Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### Warning

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**Indications:** When the combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium sparing action of triamterene is warranted. (See Box Warning.) Routine use of diuretics in healthy pregnant women is inappropriate; they are indicated in pregnancy only when edema is due to pathological causes.

**Contraindications:** Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K<sup>+</sup> levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K<sup>+</sup> intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids).

Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K<sup>+</sup> frequently; both can cause K<sup>+</sup> retention and elevated serum K<sup>+</sup>. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis.

'Dyazide' interferes with fluorescent measurement of quinidine.

### Adverse Reactions:

Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions;

nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

**FOR LONG-TERM CONTROL  
OF HYPERTENSION\*  
SERUM K<sup>+</sup> AND BUN SHOULD  
BE CHECKED PERIODICALLY.  
(SEE WARNINGS SECTION.)**

SK&F CO., Carolina, P.R. 00630

**SK&F CO.**  
a Smithkline company



# B.W.CO. HAS PUT MORE POTENCY IN THE LINE



**EMPRACET® with Codeine Phosphate, 60 mg, No. 4 ©**

**EMPRACET® with Codeine Phosphate, 30 mg, No. 3 ©**

**CONTRAINDICATIONS:** Hypersensitivity to acetaminophen or codeine.

**WARNINGS:** **Drug dependence.** Codeine can produce drug dependence of the morphine type and may be abused. Dependence and tolerance may develop upon repeated administration; prescribe and administer with same caution appropriate to oral narcotics. Subject to the Federal Controlled Substances Act.

**Usage in ambulatory patients.** Caution patients that these products may impair mental and/or physical abilities required for performance of potentially hazardous tasks such as driving a car or operating machinery.

**Interaction with other CNS depressants.** Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, tranquilizers, sedative-hypnotics, or other CNS depressants (including alcohol) may exhibit additive CNS depression; when used together reduce dose of one or both.

**Usage in Pregnancy.** Safe use is not established. Should not be used in pregnant patients unless potential benefits outweigh possible hazards.

**PRECAUTIONS:** **Head injury and increased intracranial pressure.** Respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

**Acute abdominal condition.** These products or other narcotics may obscure the diagnosis or clinical course of acute abdominal conditions.

**Special risk patients.** Administer with caution to certain patients such as elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, or prostatic hypertrophy or urethral stricture.

**ADVERSE REACTIONS:** Most frequently include lightheadedness, dizziness, sedation, nausea, and vomiting; more prominent in ambulatory than in nonambulatory patients; some may be alleviated if patient lies down; others include: euphoria, dysphoria, constipation and pruritus.

**DRUG INTERACTIONS:** CNS depressant effect may be additive with that of other CNS depressants. See Warnings.

For symptoms and treatment of overdosage and full prescribing information, see package insert.

## Introducing **EMPRACET®** **© CODEINE #4**

Each tablet contains: codeine phosphate,  
60 mg (1 gr) (Warning—may be habit-forming);  
and acetaminophen, 300 mg.



## Our new non-aspirin/ codeine analgesic for moderate to severe pain.

New peach-colored Empracet © Codeine #4 offers a potent alternative for patients in whom aspirin is not indicated.

Unlike compounds containing oxycodone which afford comparable analgesia, new Empracet © Codeine #4 gives you CIII prescribing convenience—up to 5 refills in 6 months at your discretion (where state law permits). And, prescribing by telephone is permissible in most states. Moreover, new Empracet © Codeine #4 has less addiction potential than does oxycodone.

For those of your patients requiring a less potent analgesic, non-aspirin Empracet® © Codeine #3 provides effective relief of moderate pain.

**Burroughs Wellcome Co. makes codeine combination products. You make the choice.**



**Burroughs Wellcome Co.**  
Research Triangle Park  
North Carolina 27709



### *PAYING TODAY GIVES PATIENTS A PAIN*

Has this scene occurred lately in your office?

"Mr. Patient, that will be \$25.00 for today's visit," says your medical assistant.

Angry and red-faced Mr. Patient replies, "Well I've always paid my bill here. Why don't you just send me a statement like you always do?"

"Because, sir, this is our new policy," your assistant curtly replies.

Meanwhile, all the patients in the reception room have put down Newsweek, Ladies Home Journal, and last year's copy of Ski magazine. They are sitting at the end of their chairs, eagerly listening to see how Mr. Patient is going to get out of this and wondering how they'll handle the situation when they're confronted with their bill for your services.

Embarrassed, Mr. Patient, tells the assistant he doesn't have his checkbook and he leaves with her calling out "But don't forget next time!"

Well, the truth is there may not be a next time. Mr. Patient may decide to go elsewhere for his medical care.

But this doesn't have to be the case. If your office is one of the many all across the country now asking patients to pay for their office visits on the same day you can implement the policy successfully and still keep your patients happy by following a few easy procedures.

First, we recommend that you send all of your established patients a letter explaining the new policy. It will help reduce long telephone explanations for your assistants and eliminate the surprise factor that so many patients resent. Send the letter on your stationery about two to three months before implementing the policy. It might say something like this.

Dear Patient,

Inflation is a growing problem for everyone, including medical offices. Today we find ourselves confronted with ever-increasing costs for almost every supply and service we use in rendering professional care to you.

Rather than raise our fees now, which we may have to do from time to time, we are asking your help in a new cost-cutting plan. Beginning on (give a date two to three months in advance) we will ask you to pay for your office call at the time of your visit. By asking you to do this we can significantly reduce the costs of billing and bookkeeping.

We understand that occasions may arise when it will be necessary for you to ask for a statement rather than paying at the time of service. We also recognize, as we always have that patients who require extensive treatment may need payment plans.

We wanted to explain this new system to you well in advance because your understanding and cooperation are so important. Please remember that if you have questions about this or any other office policy or procedure we will be pleased to discuss them with you. We value you, our patient, and will continue to provide you with our best professional care.

Sincerely,

XYZ Medical Office

But your patient relations effort shouldn't stop here. Next, you and your front office personnel need to discuss how firm you plan to be and this varies from office to office. In any case, your medical assistants need to know what you're thinking is on this topic and be assured that you're going to back them up. (No fair for the doctor to tell patients "not to worry about the bill" if they ask about your fees in the examining room unless you *mean* just that!)

Your medical assistants should also make a point of reminding patients of the new policy when they call to make an appointment. For example they can say, "Mrs. Black, we have you scheduled for next Tuesday at 2:00 p.m. Your office visit will be \$10.00 and any lab work the doctor orders will be extra." If Mrs. Black objects, your assistant can remind her about the letter and that this request is being made of all patients. If Mrs. Black says she won't be able to pay, your assistant should probably go ahead and

keep the appointment for her and tell her she's making a note of the agreement to send a statement on Mrs. Black's ledger card. Later, you or your bookkeeper may want to have a private conversation with Mrs. Black if she persists in being an exception to the rule.

Office layout and design also play a part in making this policy work successfully. It's going to be much easier, if you have a separate check out counter, away from the reception room or an area that gives your assistant and the patient some degree of privacy. It will allow the patient to give an honest explanation of their circumstance and your assistant the ability to make some arrangement to suit that patient's needs without curious eyes and ears, looking and listening. If you need to build a wall or install a door, do so. It's going to be worth the investment.

How should your assistant ask for payment? That depends on you. Offices taking the more flexible approach, simply have the assistant say, "Mr. Patient, your visit today is \$15.00 or, "Mr. Patient, your visit is \$15.00 and we invite payment today." The office that is willing to take a more aggressive approach has the assistant say, "Mr. Patient, your visit today is \$15. "Would you like to pay by cash or check?" Both are better techniques than simply saying, "Your visit today is \$15.00, would you like to pay?" No one would *like* to pay today-- anywhere, anytime, including your office! This simply invites, the "send me a bill" response.

Now, what happens if the patient says, "Gee, you know I always try to come prepared, but today, I forgot my checkbook." That's going to happen sometimes, and your assistant should be prepared. She should say, "Miss Patient, that's okay, we understand, here's your statement and an *envelope* please mail your payment, just as soon as you can." Most offices report that they receive payment in a few days, without ever having to send a bill. You might make that return envelope a color so it's easy to spot when the payment comes in.

The important thing to keep in mind about asking for payment at the time of service is good patient relations and that you're going to have to make exceptions. With these two thoughts in mind, you're sure to succeed, without giving your patients a new pain.

By Karen Zupko, Program Director  
Department of Practice Management  
Division of Medical Practice  
American Medical Association

JANUARY 23-28, 1978. *FIFTH ANNUAL NEUROLOGICAL UPDATE*. Miami Beach, Florida. Sponsored by the Department of Neurology, University of Miami School of Medicine. A.M.A. accredited. Adult Neurology, 4-1/2 days, 25 hrs.; Child Neurology, 1-1/2 days, 8 hrs.; combined program, 6 days, 33 hrs. Director: Peritz Scheinberg, MD. Information: Division of Continuing Medical Education, University of Miami School of Medicine, P. O. Box 520875, Miami FL 33152. Tel. (305) 547-6716.

---

#### FROM THE NATIONAL COMMISSION ON DIGESTIVE DISEASES.

##### Announces Plans for Public Hearings:

The National Commission on Digestive Diseases has announced plans to conduct public hearings across the country to develop information on one of the nation's major, but often overlooked, health problems.

The first hearing is scheduled in New York City Oct. 11 at Memorial Sloan Kettering Cancer Center. The second is slated at the New Jersey College of Medicine and Dentistry, Oct. 12. Other hearings are planned in Chicago, Denver, Houston, Seattle, Los Angeles, Florida, and Washington, D. C.

Diseases of the organs making up the digestive system affect nearly 18-million Americans with consequent economic costs approaching 11 billion dollars annually.

Congress, concerned over the medical, social, and economic implications of widespread digestive diseases, established the Commission and directed it to develop and submit by October, 1978, a long-range plan for the more effective use and the more efficient organization of national resources to combat digestive illnesses.

The 26-member Commission includes research scientists, medical educators, allied health professionals, and representatives of the public. The Commission chairman is Dr. Eugene D. Jacobson, Associate Dean for Basic Science and Research, University of Cincinnati College of Medicine.

In announcing the planned public hearings, Dr. Jacobson called public involvement "essential to the success of the Commission." He noted that digestive diseases are a leading cause of hospitalization in the nation's population, the second major cause of disability and days lost from work, the third leading cause of death, and ranked behind only cardiovascular diseases as a cause of visits to physicians.

He said the 26 members of the Commission intend to participate fully in the hearings and "are anxious to hear the testimony of scientists, nurses, practicing physicians, hospital staff and administrators, medical educators, medical students, allied health professions, officials at all levels of government, and those people representing organizations dedicated to the welfare of victims of digestive diseases."

"But most especially," he emphasized, "the Commission would like to hear from the people who pay the price in pain — the patients and their families."

Hearings will be informal, but written testimony is requested and the time of individual witnesses may be limited to accommodate all those seeking to testify.

The Commission has its offices in Bethesda, Md., and further information on the hearings and on the work of the Commission may be obtained from Dr. Thomas P. Vogl, Executive Secretary, National Commission on Digestive Diseases, Federal Building, 7550 Wisconsin Avenue, Bethesda, Md. 20014 (301) 496-1347.

---

#### COMUNICACION RECIBIDA DEL NATIONAL INSTITUTE OF HEALTH:

"Physicians across the country have long felt the need for greater clarity in the approach to the treatment of high blood pressure and for guidance in the management and the education of hypertensive patients. The Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure answers these needs. This Report marks the first time representatives of major medical associations have reached a consensus on hypertension management.

One of the most important features of this Report is its simple, economic approach to diagnosis and treat-

ment. Blood pressures are specified as requiring further investigation, periodic follow-up, or treatment. Updated guidelines for therapy have been formulated. The Report presents a pharmacologic rationale for the "step-care" approach to therapy. The Report also offers guidance in increasing compliance through patient education and through approaches to patient management.

Orders for this important publication are being taken now. It will be available in August. We encourage you to inform members of your state and county medical society about it by announcing its availability in your state medical journal for the convenience of your members, if you wish.

Copies of the Joint National Committee Report may be ordered from the High Blood Pressure Information Center, 120/80 National Institutes of Health, Bethesda, Maryland 20014."

---

#### LISTA DE OBRAS PROCESADAS — UNIVERSIDAD DE PUERTO RICO - RECINTO DE CIENCIAS MEDICAS — BIBLIOTECA, DEPARTAMENTO DE SERVICIOS TECNICOS, JUNIO, 1977.

##### ALERGIA:

Somekh, Emile. A parent's guide to children's allergies. 1972. (WD 300 SoI 1972)

##### CIRUGIA:

American College of Surgeons. Committee on Pre and Postoperative Care. Manual of surgical nutrition. 1975. (WO 178 AmI 1975)

Bailey, Hamilton. Demonstrations of physical signs in clinical surgery. 15th ed. 1973. (WO 141 BaXV 1973)

Ferguson, Lewis Kraeer. Surgery of the ambulatory patient. 5th ed. 1974. (WO 192 FeV 1974)

Hewer, Christopher Langton. Recent advances in anaesthesia and analgesia. 12th ed. 1976. (WO 200 HaXII 1976)

Nixon, Harold. The essentials of paediatric surgery. 3rd. ed. 1976. (WO 925 NiIII 1976)

Principles of surgery. Editor-in-chief: Seymour I. Sch-



- wartz, 2d ed. 1974. (WO 100 PrII 1974)  
 Shock, clinical and experimental aspects. Edited by Iain McA. Ledingham. 1976. (WO 149 Shi 1976)  
 Zollinger, Robert. Atlas of surgical operations. 4th ed. 1975. (WO 17 ZoIV 1975)

## DERMATOLOGIA:

- Braverman, Irwin H. Manifestaciones cutáneas de las enfermedades sistémicas. 1973. (WR 140 BrI 1973)

## EDUCACION MEDICA:

- Costa Rica. Universidad. Antecedentes, planes y primeras realizaciones, para el establecimiento de la Escuela de Medicina. 1957. (W 19 CoI 1957)  
 The Future of medical education by William G. Anlyan et al. 1973. (W 18 FuI 1973)  
 The Future role of university-based metropolitan medicine centers. 1972. (W 18 FuI 1972)  
 Institute on International Medical Education, Washington, D. C., 1966. Manpower for the world's health. Ed. by Henry van Zile Hyde. 1966. (W 18 InI 1966)

## ENDOCRINOLOGIA:

- Diabetes mellitus por Profesor Dr. med. Platon Petrides et al. 1974. (WK 810 DiI 1974)  
 Gastrointestinal hormones; international symposium at Erlangen, August 1971. Edited by Ludwig Demling. 1972. (WK 170 GaI 1972)

## ENFERMEDADES CARDIOVASCULARES:

- Advances in cardiovascular surgery. Edited by John W. Kirklin. 1973. (WG 168 AdI 1973)  
 Advances in electrocardiography, by J. A. Abildskov et al. 1972. (WG 140 AdI 1972)  
 Chou, Te-Chuan. Clinical vectorcardiography. 2d ed. 1974. (WG 140 ChII 1974)  
 Cosby, Richard S. Los bloqueos cardíacos. Versión española de P. Marsé Millá. 1974. (WG 330 CoI 1974)  
 Goldberger, Emanuel. Urgencias cardíacas y su tratamiento. Versión española de A. Coveio Peredeiro. 1976. (WG 205 GoI 1976)  
 Hollenberg, Norman K. Directions in cardiovascular medicine; the kidney in congestive heart failure; sodium homeostasis, renal hemodynamics and nephron function, by Norman K. Hollenberg and Paul J. Can-

- non. 1975. (WG 370 HoI 1975)  
 Hurst, John Willis, ed. The heart, arteries and veins. 3d ed. 1974. (WG 100 HuII 1974)  
 Kidd, B. S. Langford, ed. The child with congenital heart disease after surgery. 1976. (WG 220 KiI 1976)  
 Kones, Richard J. Shock cardiogénico. 1976. (WG 300 KoI 1976)  
 Owen, Samuel Griffith. Electrocardiografía. 1974. (WG 140 OwI 1974)  
 Soldati, León de. Enfermedades cardiovasculares. 1970. (WG 100 SoI 1970)  
 Simposio sobre el Fallo Mecánico del Corazón, Santiago de Chile, 1972. El fallo mecánico del corazón. Editada bajo la dirección de Pedro Zarco y Jaime Pérez-Olea. 1975. (WG 370 SiI 1975)

## ENFERMEDADES METABOLICAS:

- Duncan, Garfield George, ed. Diseases of metabolism. 7th ed. 1974. (WD 200 DuVII 1974)  
 Goldberger, Emanuel. A primer of water, electrolyte and acid-base syndromes. 5th ed. 1975. (WD 200 GoV 1975)  
 Robinson, James Roper. Fundamentals of acid-base regulation. 5th ed. 1975. (WD 220 RoV 1975)

## ENFERMEDADES RESPIRATORIAS:

- Cherniack, Reuben M. Respiración normal y patológica. 2d ed. 1974. (WF 140 ChII 1974)  
 Cole, R. B. Essentials of respiratory disease. 2d ed. 1975. (WF 140 CoII 1975)

## FISIOLOGIA:

- Ganong, William F. Review of medical physiology. 7th ed. 1975. (QT 4 GaVII 1975)  
 Jensen, J. Trygve. Physics for the health professions. 2d ed. 1976. (QT 34 JeII 1976)  
 Selkurt, Ewald E., ed. Physiology. 4th ed. 1976. (QT 4 SeIV 1976)

## GASTROENTEROLOGIA:

- Badenoch, John, ed. Recent advances in gastroenterology. 2d ed. 1972. (WI 100 BaII 1972)  
 Ilfter, Ernst. Gastroenterología práctica. 2a ed. 1976. (WI 100 HaII 1975)

International Symposium on Gastrointestinal Motility, 4th, Banff, Alta., 1973. Proceedings. Edited by E. E. Daniel et al, 1974. (WI 102 InI 1974)

Schiff, Leon. ed. Diseases of the liver. 4th ed. 1975. (WI 700 ScIV 1975)

Truelove, Sidney Charles, ed. Problemas gastroenterológicos. 1975. (WI 100 TrI 1975)

#### HEMATOLOGIA:

Advances in acute leukemia. Edited by F. J. Cleton, D. Crowther and J. S. Malpas. 1974. (WH 250 AdI 1974)

Brown, Barbara A. Hematology: principles and procedures. 2d ed. 1975. (WH 25 BrII 1975)

#### INMUNOLOGIA:

Holborow, E. J. Inmunología fundamental. 1974. (QW 504 HoI 1974)

Immunology for surgeons. Edited by J. E. Castro. 1976. (QW 504 ImI 1976)

#### MEDICINA INTERNA:

Davidson: principios y práctica de la medicina. Editado bajo la dirección de John Mcleod y colaboradores. 1976. (WB 100 DaI 1976)

Guidelines for selection and appraisal of diagnostic tests. 1971. (WB 141 GuI 1971)

Harrison, Tinsley Randolph, ed. Principles of internal medicine. 7th ed. 1974. (WB 100 HaVII 1974)

Judge, Richard D., ed. Methods of clinical examination. 3d ed. 1974. (WB 200 JuIII 1974)

Prior, John A. Physical diagnosis; the history and examination of the patient. 4th ed. 1973. (WB 200 PrI 1973)

Stevenson, Ian P. La historia clínica. 1974. (WB 290 StI 1974)

#### NEUROLOGIA:

Barraquer-Bordás, Luis. Afasias, apraxias, agnosias. 2d ed. 1976. (WL 340 BaII 1976)

Critchley, Macdonald, ed. Scientific foundations of neurology. 1972. (WL 100 CrI 1972)

Eccles, John Garew. The understanding of the brain. 1973. (WL 300 EcI 1973)

Guyton, Arthur Clifton. Structure and function of the nervous system. 2d ed. 1976. (WL 102 GuII 1976)

Lance, James W. A physiological approach to clinical neurology. 2d ed. 1975. (WL 102 LaI 1975)

McDowell, Fletcher Hughes. Enfermedades vasculares cerebrales. 1975. (WL 355 MaI 1975)

Walton, John Nicholas. Essentials of neurology. 4th ed. 1975. (WL 100 WaIV 1975)

#### OBSTETRICIA Y GINECOLOGIA:

Benson, Ralph Criswell. Handbook of obstetrics and gynecology. 5th ed. 1974. (WP 100 BeV 1974)

Cervical mucus in human reproduction. Edited by Max Elstein, Kamran S. Moghissi and Rudi Borth. 1973. (WQ 205 CeI 1973)

Coppleson, Malcolm. Colposcopia. 1974. (WP 480 CoI 1974)

Goecke, Claus. Ginecología fundamental. 1974. (WP 100 GoI 1974)

Guido, Clemente. Temas ginecológicos. 1975. (WP 100 GuI 1975)

Novak, Emil. Gynecologic and obstetric pathology, with clinical and endocrine relations. 7th ed. (WP 140 NoVII 1974)

Speroff, Leon. Endocrinología ginecológica e infertilidad. 1975. (WP 505 SpI 1975)

#### OFTALMOLOGIA:

Geeraets, Walter Jean. Ocular syndromes. 3d ed. 1976. (WW 475 GeIII 1976 Ref.)

Hochberg, Julian E. La percepción. 1968. (WW 103 HoI 1968)

Kolker, Allan E. Diagnóstico y tratamiento del glaucoma. 2d ed. 1975. (WW 290 KoII 1975)

Newell, Frank, William. Ophthalmology. ed ed. 1974. (WW 100 NeIII 1974)

Pediatric ophthalmology. Edited by Robinson D., Harley. 1975. (WW 100 PeI 1975)

Recent advances in ophthalmology. Edited by P. D. Trevor-Roper. 5th ed. 1975. (WW 100 ReV 1975)

#### ORTOPEDIA:

Debrunner, Hans Ulrich. Diagnóstico ortopédico. 2d ed. 1976. (WE 168 DeII 1976)

Pannike, Alfred. Osteosíntesis en la cirugía de la mano. 1974. (WE 830 PaI 1974)

Smith, Frederick M. Cirugía del codo. 1976. (WE 820 SmI 1976)

Veigel, Burkhart. Prótesis de la articulación de la cadera. 1976. (WE 860 VeI 1976)

#### OTORRINOLARINGOLOGIA:

Dublin, William Brooks. Fundamentals of sensorineural auditory pathology. 1976. (WV 250 DuI 1976)

Pracy, R. A short textbook: ear, nose and throat. 2d ed. (WV 100 PrI 1976)

Wright, Mary Ingle. The pathology of deafness. 1971. (WV 270 WrI 1971)

#### PATOLOGIA:

Dyke, Sidney Campbels, ed. Recent advances in clinical pathology. 6th ed. 1973. (QY 4 DyVI 1973)

Follow-up of cancer. Sponsored by Connecticut State Medical Society and the American Cancer Society, Connecticut Division. 1974. (QZ 200 FoI 1974)

Oppenheim, Irwin A. Textbook for laboratory assistants. 2d ed. 1976. (QY 25 OpII 1976)

Robbins, Stanley L. Basic pathology. 2d ed. 1971. (QZ 4 RoII 1976)

Sans-Sabrafen, J. Manual de quimioterapia antineoplásica. 1976. (QZ 267 SaI 1976)

Sodeman, William Anthony. Pathologic physiology. 5th ed. 1974. (QZ 140 SoV 1974)

#### PEDIATRIA:

Blanco, Ralph F. Prescriptions for children with learning and adjustment problems. 1972. (WS 350 B&I 1972)

Current problems in pediatric hematology. Edited by Frank A. Oski, Ernst R. Jaffé and Peter A. Miescher. 1975. (WS 300 CuI 1975)

Duche, Didier J. La enuresis: formación de hábitos higiénicos en los niños. 1972. (WS 350 DuI 1972)

Ford, Frank Rodolph. Diseases of the nervous system in infancy, childhood, and adolescence. 6th ed. 1973. (WS 340 FoVI 1973)

Overbach, Arvin M. Drugs used with neonates and during pregnancy. 1975. (WS 366 OvI 1975 Ref.)

Simmons, James E. Psychiatric examination of children. 2d ed. 1974. (WS 350 SiII 1974)

Williams, David Innes, ed. Paediatric urology. 1968. (WS 320 WiI 1968)

#### PROFESIONES MEDICAS Y RELACIONADAS:

Bernstein, Lewis. Interviewing. 2d ed. 1974. (W 62 BeII 1974)

Fendall, N. R. E. Los auxiliares en el cuidado de la salud. 1975. (W 21.5 FeI 1975)

Josiah Macy, Jr. Foundation, New York. Physicians for the future. 1976. (W 76 JoI 1976)

Piulachs Oliva, Pedro. La enfermedad y el enfermo. 2a ed. 1976. (W 61 PiII 1976)

#### PSIQUIATRIA:

Freedman, Alfred M. Modern synopsis of comprehensive textbook of psychiatry, II. 1976. (WM 100 FrII 1976)

López-Ibor Aliño, Juan José. La psiquiatría de hoy. 1975. (WM 100 LoI 1975)

Mental retardation: century of decision; report to the President, by the President's Committee on Mental Retardation. 1975. (WM 300 MeI 1975)

Willis, James. Lecture notes on psychiatry. 4th ed. 1974. (WM 100 WiI 1974)

#### RADIOLOGIA:

Radiologic technology, medical service. 1975. (WN 100 RaI 1975)

Rogers, Andrew W. Techniques of autoradiography. 2d rev. and enlarged ed. 1973. (WN 445 RoII 1973)

Squire, Lucy Frank. Fundamentals of radiology. Rev. ed. 1975. (WN 100 SqII 1975)

#### L I S T A D E A N U N C I A N T E S

BOEHRINGER INGELHEIM ----- TORECAN  
BURROUGHS WELLCOME ----- CODEINE ANAL., SEPTRA  
CARNATION ----- EVAPORATED MILK  
CIBA PHARM. ----- VIOFORM - HC  
SMITH, KLINE & FRENCH ----- DYAZIDE  
UPJOHN COMPANY --- ORINASE

EATON LAB. --- FURACIN TOP.  
ROCHE LAB. --- BACTRIM, VALIUM  
ROERIG & CO. --- ANTIVERT  
RORER INT'L --- ASCRIPTIN W/COD.  
U.S.V. PHARM. --- HYGROTON



# In recurrent urinary tract infections due to susceptible organisms\*

## Septra<sup>®</sup> DS Tablets

Each tablet contains

**160 mg trimethoprim and  
800 mg sulfamethoxazole**

## Septra<sup>®</sup> Suspension

Each teaspoonful (5 ml) contains

**40 mg trimethoprim and  
200 mg sulfamethoxazole**

## In vitro antibacterial action well balanced by clinical success

- convenient b.i.d. dosage schedule helps insure patient compliance
- pleasantly flavored cherry suspension available for children
- Septra and Septra DS now available in new *small-size* tablets

## Rx guidelines

- during therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination
- contraindicated in children under two months old
- see prescribing information for complete guidelines

\*It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

## Septra<sup>®</sup>

Tablets and Suspension

**Indications and Usage: Urinary Tract Infections:** Urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37: 20527-29, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

**Precautions:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred. Due to certain chemical similarities to some

gortogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

**Dosage and Administration:** Not recommended for use in infants less than two months of age.

**Adults:** The usual adult dosage for the treatment of urinary tract infections is one double strength tablet or two regular tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

**Children:** Recommended dose is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in *two* divided doses for 10 days. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older

Weight		Dose — every 12 hours	
lb	kg	Teaspoonfuls	Tablets
20	9	1 ( 5 ml)	1/2
40	18	2 (10 ml)	1
60	27	3 (15 ml)	1 1/2
80	36	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the Usual Dosage Regimen
Below 15	Use Not Recommended

**Supplied:** Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole — bottles of 60 tablets and unit dose packs of 100. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole — bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored — bottles of 450 ml.

**References:** 1. PMR Bacteriologic Report — urine cultures only. National summary Dec 1975, Jan 1976, Feb 1976. (From 200 acute care hospitals of 100 beds or more.) Data on file, Burroughs Wellcome Co.  
2. Data on file, Burroughs Wellcome Co.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

# The Septra<sup>®</sup> B

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazole

## A strong in vitro record<sup>1</sup>

### E coli

**Septra 95%**  
of 220517 isolates

**Cephalosporin 79%**

of 358025 isolates

**Ampicillin 74%**

of 351311 isolates

**Nitrofurantoin 95%**

of 338756 isolates

### Proteus sp

**Septra 91%**  
of 66163 isolates

**Cephalosporin 81%\***

of 106281 isolates

**Ampicillin 77%\***

of 104437 isolates

**Nitrofurantoin 13%**

of 100829 isolates

\*Indicated in approved drug information  
for *Proteus mirabilis* only.

### Enterobacter

**Septra 87%**  
of 9896 isolates

**Cephalosporin 32%†**

of 14986 isolates

**Ampicillin 15%†**

of 14036 isolates

**Nitrofurantoin 66%**

of 14219 isolates

†Not indicated in approved drug information.

### Klebsiella

### pneumoniae

**Septra 87%**  
of 46279 isolates

**Cephalosporin 85%**

of 76898 isolates

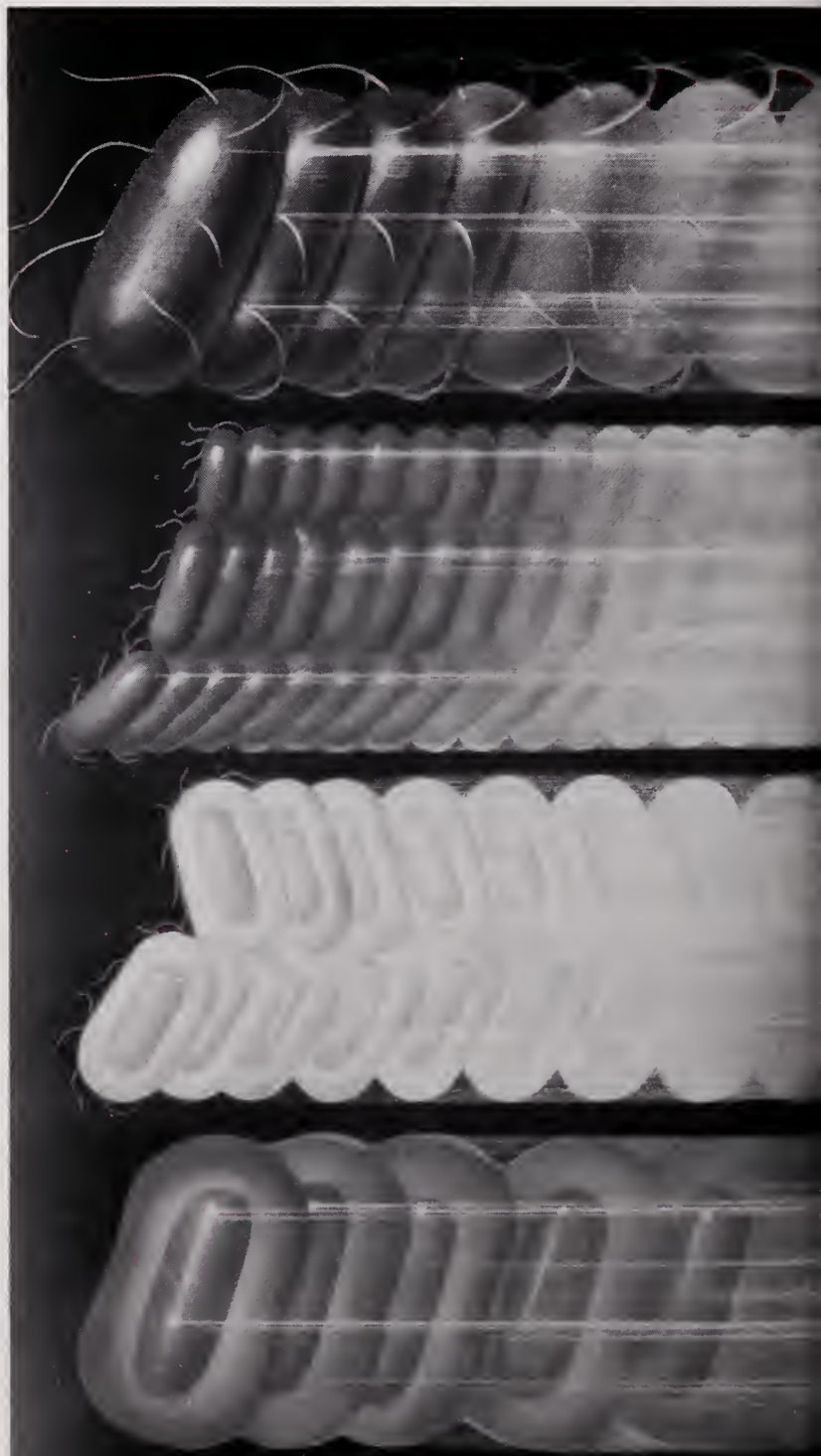
**Ampicillin 5%†**

of 76026 isolates

**Nitrofurantoin 68%**

of 72030 isolates

†Not indicated in approved drug information.



**In vitro activity does not necessarily  
imply a correlation with in vivo results.**



# ance of Power

## A consistent in vivo response

### Septra outperformed cephalixin

In a study of 148 patients with recurrent urinary tract infections,<sup>2</sup> bacteriologic response rate on day 14 of therapy<sup>††</sup> was 99% with Septra, compared to 94% with cephalixin.<sup>5</sup> This superiority of response to Septra occurred in spite of a built-in "handicap": Infecting organisms had to be susceptible *in vitro* to cephalixin, but not necessarily to Septra. Drug regimens consisted of either two Septra tablets b.i.d. or one 250 mg cephalixin pulvule q.i.d.

<sup>††</sup>Results derived from urine cultures done at the midpoint of a 28-day study, since recommended duration of Septra therapy is 14 days.

<sup>5</sup>Criterion for infection: 100,000 or more organisms/ml urine; criterion for clear culture: 1000 or fewer organisms/ml urine.

### Septra outperformed ampicillin

In a study of 10-day therapy in 156 patients with recurrent urinary tract infections,<sup>2</sup> clear culture was maintained four days after therapy ended in 81% of patients treated with Septra, compared to 76% of those treated with ampicillin.<sup>9</sup> These results gain added significance considering that causative organisms not susceptible *in vitro* to ampicillin were excluded, but no such advantage was afforded Septra. Drug regimens consisted of either two Septra tablets b.i.d. or one 500 mg ampicillin capsule q.i.d.

<sup>9</sup>Criterion for infection: 100,000 or more organisms/ml urine; criterion for clear culture: 1000 or fewer organisms/ml urine.

### Septra outperformed nitrofurantoin (macrocrystals)

In a study of 289 patients treated for 14 days for recurrent urinary tract infections,<sup>2</sup> bacteriologic response (measured eight days after therapy ended) to Septra was 94%, compared to 90% with nitrofurantoin.<sup>5</sup> Drug regimens consisted of either two Septra tablets b.i.d. or one 100 mg capsule of nitrofurantoin macrocrystals q.i.d.

<sup>5</sup>Criterion for infection: 100,000 or more organisms/ml urine; criterion for clear culture: 1000 or fewer organisms/ml urine.

### In vitro antibacterial action well balanced by clinical success

# Septra® DS

Each tablet contains:

**160 mg trimethoprim and 800 mg sulfamethoxazole  
in recurrent urinary tract infections  
due to susceptible organisms<sup>#</sup>**

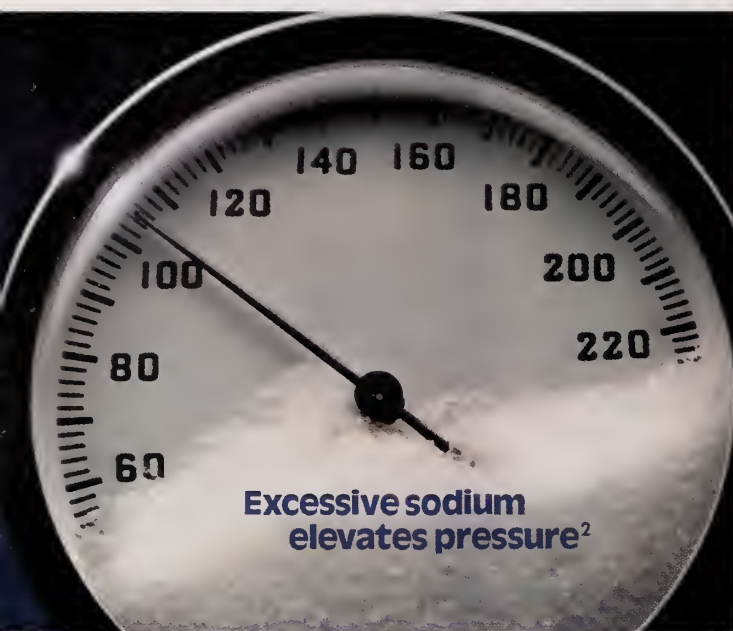
<sup>#</sup>It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

Artist's conception of major uropathogens.  
See next page for prescribing information.





# In hypertension...



Excessive sodium  
elevates pressure<sup>2</sup>

## Hygroton® 50 mg. (chlorthalidone USP)

### As step-1 therapy

Sustained control of sodium retention is important for sustained control of hypertension. Hygroton blocks sodium retention longer than any other diuretic available.

### As baseline diuretic in step-2 therapy

Reserpine, methyldopa and propranolol may cause compensatory sodium retention. For this reason, the National Task Force<sup>1</sup> recommends diuretics as the baseline in step-2 therapy. Hygroton is an "ideal" choice because of its sustained blockade of sodium retention.

# Hygroton® 50 mg. one a day (chlorthalidone USP) Blocks sodium retention longer

#### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema.

**Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug

may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance.

**Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn.

**Usual Dose:** One tablet daily

**How Supplied:** Tablets — 100 mg. (white, scored) and 50 mg. (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6

#### References:

1. Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure: A Cooperative Study, JAMA 237:255, January 17, 1977.
2. Laragh, J.H. et al. Vasoconstriction — volume analysis for understanding and treating hypertension. The use of renin and aldosterone profiles, in Hypertension Manual (Laragh, J.H., ed.), New York, Dun-Donnelley, 1974, pp 824-825.

**USV  
LABORATORIES**

USV Laboratories Inc.  
Manati, P.R. 00701



Continues to kill Staph. aureus  
and other burn wound invaders...

## **Furacin<sup>®</sup>** soluble dressing (nitrofurazone) for dressing and re-dressing second- and third-degree burns

With the constant advent of new antibacterials, resistance patterns change...but today, as in 1947, Furacin (nitrofurazone) continues to be bactericidal against *Staph. aureus*, the most common burn wound invader, and one which frequently develops resistance to other antibacterials. Furacin is also bactericidal against most other bacteria commonly causing surface infection.

Furacin is painless and soothing on application, water-soluble, nonmacerating, and virtually nontoxic to tissue.

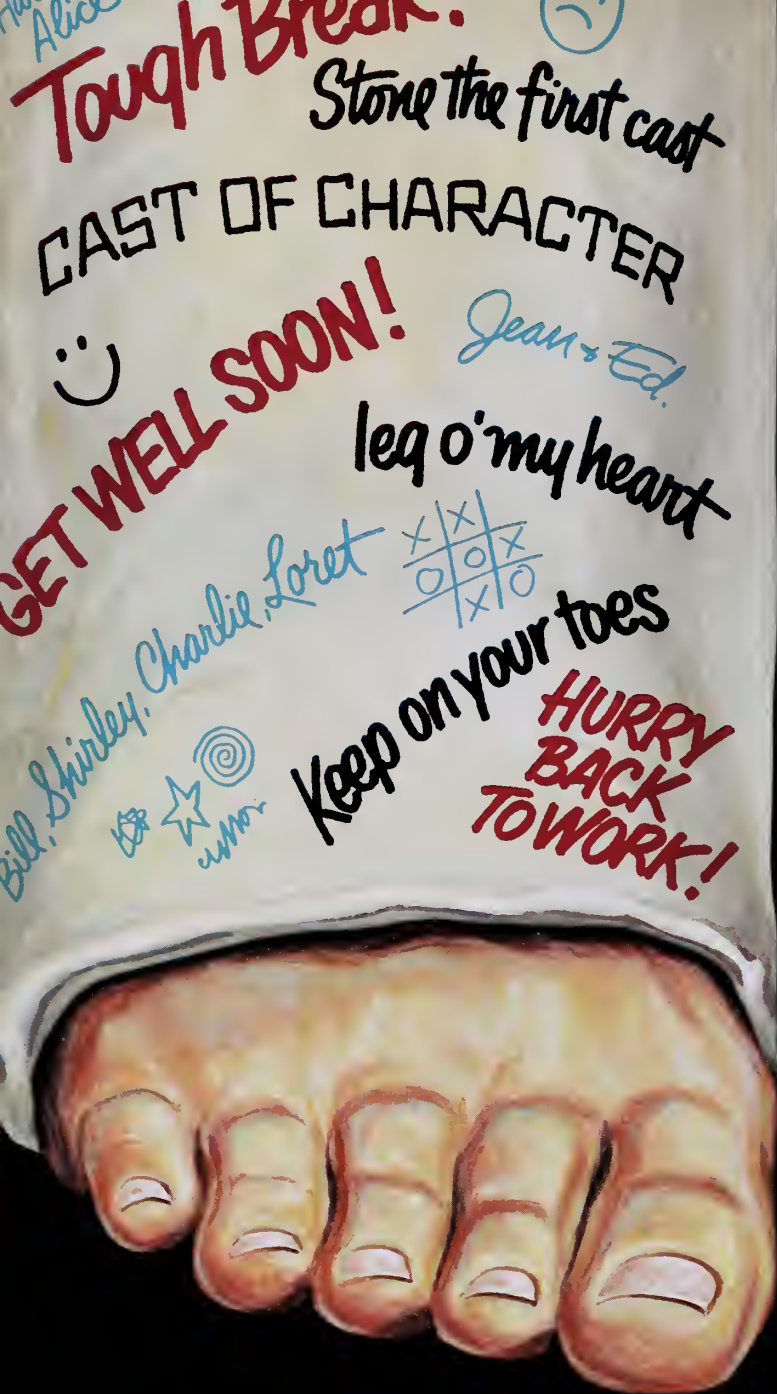
Furacin is available in tubes of 28 grams and 56 grams, and jars of 135 grams, 454 grams, and 5 pounds.

**Contains:** 0.2% Furacin (nitrofurazone). **Indications:** Adjunctive therapy for 2nd and 3rd degree burns when bacterial resistance to other agents is a real or potential problem. Skin grafting where bacterial contamination may cause graft rejection and/or donor site infections. **Contraindications:** Known prior sensitization to nitrofurazone. **Warnings:** Nitrofurazone has been shown to produce mammary tumors when fed at high doses to female Sprague-Dawley rats. The relevance of this to topical use in humans is unknown. **Safe use of nitrofurazone during pregnancy** has not been established. Use on women of child-bearing age is not recommended unless the therapeutic benefit outweighs the possible risk. **Precautions:** As with other topical antimicrobial agents, overgrowth of resistant organisms may occur. If this occurs, or if irritation, sensitization or superinfection develop, treatment with nitrofurazone should be discontinued and appropriate therapy instituted. **Adverse Reactions:** Furacin has not been significantly toxic in man by topical application. Sensitivity is low, with an overall incidence of 1.1 percent. Sensitivity reactions should be handled in a normal manner, except in the rare instance of severe contact dermatitis, when steroid administration may be indicated.



**EATON LABORATORIES**  
Norwich International  
410 Park Avenue, New York, N.Y. 10022, U.S.A.





**When pain  
breaks in...  
you've got a  
fast answer.**

**for fast relief of severe pain...  
with Maalox<sup>®</sup> protection.**

# Ascriptin<sup>®</sup>

## with Codeine

No. 2— $\frac{1}{4}$  Grain Codeine Tablets  
No. 3— $\frac{1}{2}$  Grain Codeine Tablets  
no phenacetin—no caffeine

### Two dosage strengths:

No. 2 Tablet—  
 $\frac{1}{4}$  grain (16.2 mg.) Codeine Phosphate  
No. 3 Tablet—  
 $\frac{1}{2}$  grain (32.4 mg.) Codeine Phosphate

**...both with five grains of  
Maalox-protected aspirin.**

Ascriptin<sup>®</sup>, an excellent analgesic, anti-pyretic, and anti-inflammatory, combined with codeine to give effective relief from severe pain with minimal aspirin-induced gastric distress. Ascriptin with Codeine contains **no phenacetin or caffeine**. Each tablet contains Maalox<sup>®</sup> (magnesium-aluminum hydroxide) 150 mg.

**Indication:** As an analgesic for the relief of pain of all degrees of severity up to that which requires morphine.

**Side Effects:** Side effects are rare. Nausea, constipation and drowsiness may occur.

**Warning**—may be habit forming.

**Usual Adult Dose:** Ascriptin with Codeine No. 2 ( $\frac{1}{4}$  grain): Two tablets every 3 or 4 hrs. when necessary.

Ascriptin with Codeine No. 3 ( $\frac{1}{2}$  grain): One or two tablets every 3 or 4 hrs. when necessary.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034



## To relieve nausea and vomiting associated with

- postoperative recovery
- radiation therapy
- chemotherapy
- acute situations

(Contraindicated in pregnancy, severe CNS depression, comatose states and in patients who have demonstrated a hypersensitivity to phenothiazines.)

## Three dosage forms with the same 10 mg dosage strength:

**Tablets**—10 mg (thiethylperazine maleate, NF)



**Suppositories**—10 mg (thiethylperazine maleate, NF)



**Injection**—10 mg/2cc ampul (thiethylperazine maleate, NF) for IM use only.



# Torecan®

(thiethylperazine)

Still available in  
Puerto Rico



**Boehringer Ingelheim**

Boehringer Ingelheim Ltd.  
Elmsford, New York 10523

**Torecan®** (thiethylperazine)

Tablets, Suppositories and Injection

**Contraindications:** Severe CNS depression, comatose states, and in patients who have demonstrated a hypersensitivity to phenothiazines (e.g., blood dyscrasias, jaundice). Because severe hypotension has been reported after the intravenous administration of phenothiazines, this route of administration is contraindicated. The drug is contraindicated in pregnancy.

**Warnings:** Phenothiazines are capable of potentiating CNS depressants as well as atropine and phosphorous insecticides. The drug may impair mental and/or physical ability required in the performance of potentially hazardous tasks such as driving a car or operating machinery.

**Postoperative Nausea and Vomiting:** When used to control postoperative nausea and vomiting in patients undergoing elective surgical procedures, restlessness and postoperative CNS depression during anesthesia recovery may occur. Possible postoperative complications of a severe degree of any of the known reactions of this class of drug must be considered. Postural hypotension may occur after an initial injection, rarely with the tablet or suppository. Do not use with epinephrine in the treatment of drug-induced hypotension as phenothiazines may induce a reversed epinephrine effect. The most suitable vasoconstrictor agents are levaterenol and phenylephrine. The use of Torecan has not been studied following intracardiac and intracranial surgery. Not recommended for use in children under 12 years of age, or in nursing mothers since safety and efficacy have not been established.

**Precautions:** Convulsions and abnormal movements such as extrapyramidal symptoms have occurred. The varied extrapyramidal symptom complex is more likely to occur in young adults and children. Extrapyramidal effects must be treated by reduction of dosage or cessation of medication. For treatment of nausea and/or vomiting associated with anesthesia and surgery, the drug should be administered by deep intramuscular injection at or shortly before the termination of anesthesia.

**Adverse Reactions:** CNS: convulsions, extrapyramidal symptoms such as dystonia, torticollis, oculogyric crisis, akathisia and gait disturbances, occasional cases of dizziness, headache, fever and restlessness have been reported. Drowsiness may occur initially on injection but is usually alleviated by a reduction in dosage. Dryness of the mouth and nose, blurred vision, tinnitus; sialorrhea and altered gustatory sensation. Peripheral edema of the arms, hands and face. Cholestatic jaundice; cerebral vascular spasm and trigeminal neuralgia have been reported occasionally. The following have occurred with phenothiazine derivatives and should be considered: agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia, pancytopenia, eosinophilia, leukocytosis; miosis, obstipation, anorexia, paralytic ileus; erythema, exfoliative dermatitis and contact dermatitis; jaundice, biliary stasis. Hypotension, rarely leading to cardiac arrest; ECG changes. Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonos, oculogyric crises, tremor, muscular rigidity, akinesia, some of which have persisted for several months or years especially in patients of advanced age with brain damage. Menstrual irregularities, altered libido, gynecomastia, weight gain; false positive pregnancy tests. Urinary retention, incontinence; fever, laryngeal edema and angioneurotic edema, asthma. Hyperpyrexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. ECG changes. While there is no evidence that ECG changes are in any way precursors of any significant disturbance of cardiac rhythm, sudden and unexpected deaths apparently due to cardiac arrest have been reported in a few instances in hospitalized psychotic patients previously showing characteristic ECG changes. A peculiar skin-eye syndrome, which is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea, has also been recognized as a side effect following long-term treatment. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported.

**Drug Interactions:** Phenothiazines are capable of potentiating CNS depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorous insecticides. The drug may induce a reversed epinephrine effect on occasion.

For complete details, please see full prescribing information.



**We've been delivering for  
four generations--and still cost less.**

Carnation Evaporated Milk formulas have been raising strong, healthy babies since 1899—delivering the good, sound, natural nutrition newborns and infants thrive on. You see, Carnation Evaporated Milk has naturally occurring protein with all other

nutrients intact. You indicate vitamins, iron and carbohydrates to meet each baby's needs.

Importantly, a whole formula made with Carnation Evaporated Milk still costs new mothers less than any other. Carnation Evaporated Milk...for four generations. The babies under your care will thrive on it, too.



**FREE!** Send for sample copies of these informative patient oriented booklets: "Preparing Your Baby's Formula," "You and Your Contented Baby". Mail to: Carnation Company, GPO Box 682, San Juan, Puerto Rico 00936.

Name \_\_\_\_\_  
Address \_\_\_\_\_  
City \_\_\_\_\_  
State \_\_\_\_\_ Zip \_\_\_\_\_

Proximate analysis (per 100g): Moisture 73.7g;  
Fat 7.9g; Protein 7.0g; Ash 1.5g; Carbohydrate 9.9g;  
Calories 138; Vitamin A 320 IU; Vitamin D 79 IU.  
CARNATION® EVAPORATED MILK, CARNATION COMPANY  
LOS ANGELES, CA 90036.

# ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES



1902 1977  
*75<sup>to</sup>*  
*Aniversario*

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET

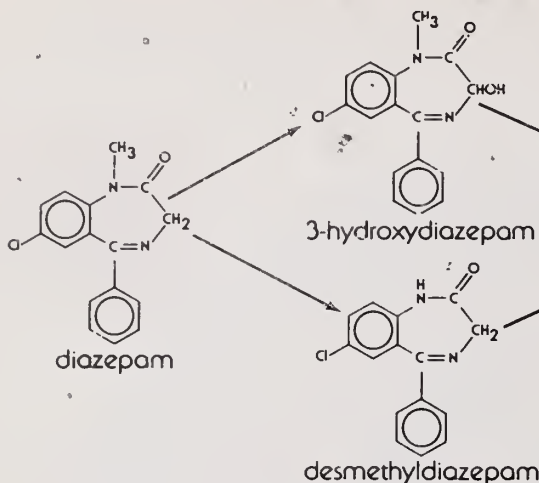
VOL. 69

Octubre 1977

No.10



# A pharmacokinetic character all its own



**Valium (diazepam) is a benzodiazepine with a distinctive pharmacokinetic profile**

The pharmacokinetic profile of Valium is one of the characteristics that sets it apart from other benzodiazepines. Consider, in particular, the metabolic pathway of Valium. The three major metabolites of Valium exhibit significant pharmacologic activity—and so, of course, does the parent substance—diazepam itself. All combine to produce the characteristic clinical response seen with Valium. The response you have come to know, to want and to trust.

Pharmacokinetic studies also demonstrate that Valium has a pattern of absorption, distribution, metabolism and elimination that is reliable and consistent. And, although the pharmacokinetics of a drug cannot, at present, be specifically related to its clinical effects, it is clearly a factor that distinguishes one product from another by providing important insights into how each moves through the patient's body.

## Valium® (diazepam) <sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due

to reflex spasm to local pathology, spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:**

Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma;

may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients.

Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

# If the AMA didn't speak for the profession, who would?

Who would speak for the profession on the 2,500 health bills introduced in every Congress? Or the regulations issued by federal agencies?

Who would state the profession's views on national health insurance? Utilization Review Regulations? The Health Planning Act of 1974? Maximum Allowable Cost Regulations? Health Manpower?

Who would provide the scientific input and the practitioner's experience and knowledge so essential to legislation on drugs, cancer, heart disease, communicable diseases? Can you think of anyone?

The fact is, there is only one organization that can — and does — speak for the profession as a whole. The AMA.

It does so to protect the basic freedoms of medical practice in any federal health program that might be enacted; and even more important, to promote legislation for better health care for the entire public.

The AMA's voice can only be as strong as the members of the profession choose to make it. With your support, the AMA can be even more effective spokesman.



**Join us.  
We can do much more together.**

Dept. of Membership Development  
American Medical Association  
535 N. Dearborn St./Chicago, IL 60610

Please send me more information on the AMA and AMA membership.

Name \_\_\_\_\_

Address \_\_\_\_\_

City/State/Zip \_\_\_\_\_

**antifungal**

**antipruritic**

**antibacterial**

**anti-  
inflammatory**



**TAXI**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform®-Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform®-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo.

Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

This product is not for ophthalmic use. In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Use in Pregnancy

Though topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm.

**Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propyleneglycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce.

**Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

Consult complete product literature before prescribing.

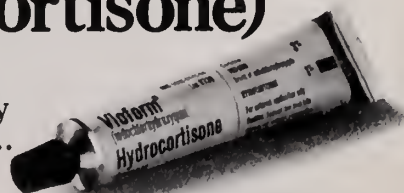
CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/6867 17

# Vioform®-Hydrocortisone

## (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

Organo Oficial

Fundado en 1903

Volumen 69

Octubre 1977

Número 10

### JUNTA EDITORA

José L. Cangiano, Presidente; Juan M. Aranda; Ramón H. Bernúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman I. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxó; Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesús M. Vázquez; Rafael Villavicencio Jiménez.

### SECRETARIO DE REDACCION

Sr. Gregorio Díaz

TODO MATERIAL SOMETIDO A ESTA PUBLICACION DEL BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO PUEDE SER FOTOCOPIADO PARA PROPOSITOS EDUCACIONALES Y CIENTIFICOS NO COMERCIALES.

### Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

### Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

### Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR, cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Hematocrit Level for Puerto Rican Women (Age 20 - 40) .....	319
Abelardo Fuertes-de la Haba, MD, DPH, FACOG, Héctor Ortiz-Pérez, MD, Ishver S. Bangdiwala, PhD, FASA, and Carlos A. Roure, MD	
Pitfalls in Prescribing Additions for the Elderly .....	327
Manuel N. Miranda, MD	
Graphics .....	329
Migdalia González, MD, Julio E. Pérez, MD Guillermo Cintrón, MD, Esteban Linares, MD Edgardo Hernández, MD, Juan M. Aranda, MD	
Abstractos: Trabajos a Presentarse en la Asamblea Anual de la AMPR - Nov. 7-12, 1977 - Salón de Convenciones del Condado .....	331
Noticias .....	354

## HEMATOCRIT LEVEL FOR PUERTO RICAN WOMEN (AGE 20 – 40)

Abelardo Fuertes-de la Haba, MD, DPH, FACOG, Héctor Ortiz-Perez, MD  
Ishver S. Bangdiwala, PhD, FASA, and Carlos A. Roure, MD

**Abstract:** A study on the hematocrit value of Puerto Rican women ages 20 - 40 was performed in the Maternal Health Study Program of the University of Puerto Rico School of Medicine and compared to United States standards. The data on hematocrit values were available for 7,720 women from the study. The mean hematocrit level of these women was 36.6 percent with a standard deviation of 3.71. In the United States the average level for ages 20 to 40 is 41.8 percent. The difference in hematocrit at almost all levels within the age groups was found to be 5 or 6 points below that of the United States standards. This doesn't show a higher incidence of anemia in our Puerto Rican population but rather that this hematocrit levels could be influenced by socio-cultural and dietary differences.

It is a common belief that the hematocrit level of our people in Puerto Rico is lower than that in the United States. Nevertheless, no sys-

tematic study has so far been conducted in Puerto Rico to establish our own standards.

It is the purpose of this article to present the results of a study conducted in a specific group of women participating in the Maternal Health Study Program of the University of Puerto Rico School of Medicine, in order to provide hematocrit level distribution by ages, and to stimulate further studies of blood values in our population. A comparison is also made with the corresponding population in the United States.

This report presents hematocrit values of a group of Puerto Rico women between the ages 20 - 40 and compares them with the standards currently used in the United States. A study by the National Center for Health Statistics (7), showed that in the United States men between the ages 18 and 79 have an average of 46.6 ml. percent of hematocrit while women have 42.4 ml. percent.

### Material and Method

The hematocrit values of the Puerto Rican group were obtained according to the micro hematocrit test, which is the usual practice followed in the United States also. Two hematocrit capillary tubes were filled within 1/4 inch of the upper end of the tube with blood specimens obtained by puncture of the index finger. They

---

*From the Department of Obstetrics and Gynecology, University of Puerto Rico School of Medicine, and the Department of Graduate Studies, University of Puerto Rico.*

*Supported by a special assignment from the Puerto Rico Legislature.*



TABLE I

## Distribution of Women in Under Study by Age Group

<i>Age Group (Years)</i>	<i>Number of Patients</i>
20 - 25	2,980
26 - 30	3,677
31 - 35	1,926
36 -40	1,101
<i>TOTAL -</i>	<i>9,684</i>
<i>Average Age</i>	<i>28.4 years</i>
<i>Median Age</i>	<i>28.0 years</i>

were then sealed with plasticen, and centrifuged (International Model M. B.) for 5 minutes. Both specimens were read to the nearest percent directly from an international micri-capillary Reader, Model CK.

The two values obtained for each examinee were averaged. The mean value was then recorded as the individual's hematocrit level in percent milliliters units.

The population utilized for this study consists of 9,684 Puerto Rican women admitted between 1961 and 1969 to the Maternal Health Research Program for an experiment of contraceptive use. The women were between the ages 20 - 40, the required age group for a controlled experiment carried out to study the effect of oral and vaginal contraceptive methods (6). The data for the United States are taken from the publication by the National Center for Health Statistics (7).

#### Characteristics of Population Under Study

The women in the contraceptive experiment belonged to three clinics: 5,552 of them were from Río Piedras clinic, 988 from Caguas and 3,144 from Ponce clinic. The two groups,

(one of users of oral contraceptives and the other using vaginal methods) to which women were randomly assigned for the experiment are tested to be fairly comparable in a number of basic demographic and biological characteristics as indicated by the results of related studies made (5). Table I shows the age distribution of this population. The average age of the group is 28.4 years and the median is 28.0 years.

The family income of the population under study ranged from "no income" per week to over \$105.00 per week with a median income of \$43.00 per week, which is of about the same magnitude as the median income of Puerto Rico during the 1960's (5). Also the educational level of the group varied from "none" to over 12 years of schooling, having a median of 7 years of schooling.

It may also be noted that in a recent study conducted by Fuertes, Bangdiwala and Roure (6), it was indicated that the average hematocrit level of the women belonging to an experimental study on contraceptives for

TABLE II

Percent Age Distribution of Hematocrit Levels in Women  
of Specific Age in Puerto Rico and United States

<i>Hematocrit Level</i>	<i>Puerto Rico (Ages 20 - 40 years)</i>		<i>United States (Ages 18 - 79 years)</i>	
	<i>Relative Percent</i>	<i>Cumulative Percent</i>	<i>Relative Percent</i>	<i>Cumulative Percent</i>
<i>Under 29.0</i>	2.5	2.5		
<i>29 - 30.9</i>	4.3	6.8	0.9	0.9
<i>31 - 32.9</i>	7.7	14.5	0.9	1.8
<i>33 - 34.9</i>	16.5	31.0	1.7	3.5
<i>35 - 36.9</i>	23.7	54.7	3.5	7.0
<i>37 - 38.9</i>	21.0	75.7	7.9	14.9
<i>39 - 40.9</i>	14.2	89.9	15.1	30.0
<i>41 - 42.9</i>	5.9	95.8	22.6	52.6
<i>43 - 44.9</i>	1.9	97.7	20.6	73.2
<i>45 - 46.9</i>	2.3	100.0	14.7	87.9
<i>47 - 48.9</i>	*	100.0	7.5	95.4
<i>49 - 50.9</i>	*	100.0	3.3	98.7
<i>51 - 52.9</i>	*	100.0	0.8	99.5
<i>53 - 55</i>	*	100.0	0.5	100.0
	100.0		100.0	
<i>Sample Base</i>		(7,720)		(6,670)
<i>Mean Hct.</i>		36.6		41.8

the oral group was 36.57 and for those of the vaginal group was 36.63, showing no significant difference statistically. Also, the percentage distribution of hematocrit for the two groups was almost the same, hence it was considered justifiable to combine the results of the two and present the hematocrit level of the women having identical characteristics as representative of the population of Puerto Rico in that age-sex group and socio-economic level. A comparison is also made with corresponding data of the United States.

Results

Of the 9,684 women in the experiment, the data on hematocrit level were available for 7,720, both shown to be representative of the original population (6). The mean hematocrit level of these women was 36.60 with a standard deviation of 3.71. The range was from as low as 20 percent up to 47 percent, as is indicated in Table II. This mean compared to United States average of women is about 6 units lower. In the United States, the average level for ages 20 -

TABLE III

## Hematocrit Level for Selected Percentiles for Puerto Rico and United States Women

<i>Percentiles</i>	<i>Puerto Rico (Ages 21 - 40 years) Ml. Percent</i>	<i>United States (Ages 18 - 79 years) Ml. Percent</i>
99.0	46.4	51.7
97.5	44.8	50.0
95.0	42.4	48.5
90.0	41.0	47.0
80.0	39.5	45.5
75.0	38.9	45.1
70.0	38.3	44.5
60.0	37.4	43.5
50.0	36.6	42.5
40.0	35.8	41.5
30.0	34.9	40.5
25.0	34.5	40.2
20.0	33.9	39.5
10.0	32.0	38.0
5.0	30.2	36.0
2.5	29.0	34.0
1	26.7	31.1

40 is 41.8 percent, and the range is from about 26 to about 54 percent.

Table III compares some selective percentile values of hematocrit level of Puerto Rico and United States women. (Although the United States population is from 18 to 79, the hematocrit levels are almost the same for the population 18 - 44, Table V) and hence are directly comparable. As can be seen from the table, the median hematocrit level of Puerto Ricans is 36.6 percent compared to 42.5 percent in United States; about 6 points less at the middle. Also it can be observed that the Puerto Rican women are con-

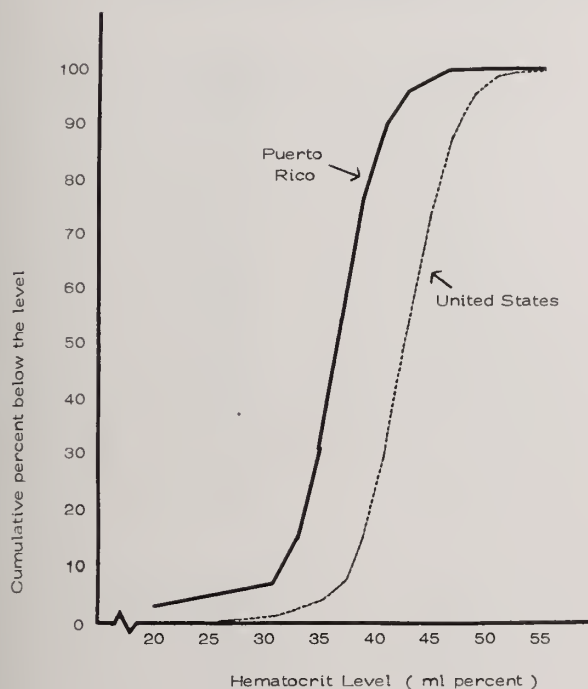
sistently 5 or 6 points lower than United States women, in general, at almost all other levels of the hematocrit reading. (See Graph I). For example, about 30 percent of the Puerto Rican women have their hematocrit level below 34.9 percent while about the same number of United States women have it below 40.5 percent. The third quartile (75 percentile value) for Puerto Rican women is 38.9 percent while for United States women it is 45.1 percent.

In Tables IV and V the distribution of the hematocrit level of women of Puerto Rico for selected age groups is compared with fairly com-



Graph I

Cumulative percent of Hematocrit Levels  
Women ( 20-40 )



parable age groups of women in the United States population. Within each of the two populations, no marked differences are indicated among various age groups. For Puerto Rican women, it is observed that for ages 21 - 25 and 26 - 30, the mean hematocrit is 36.6 percent, for ages 31 - 35 it is 36.7 percent and for ages 36 - 40 it is 36.4 percent. While the average values of hematocrit for United States women of age 18 - 24 it is 41.4 percent, for age 25 - 34 it is 41.8 percent and for ages 35 - 44 it is 42 percent. The differences at almost all levels within the age groups also is about some 5 or 6 points.

### Discussion

The hematocrit value is defined as the volume occupied by the red cells contained

in 100 ml. of blood. It is used in determining erythrocyte indices, calculations blood volume and total erythrocyte mass, and establishing whether or not the patient is anemic. It is well known, as stated earlier in this report, that the Puerto Rican population has lower hematocrit than that in the United States. It is the general practice in Puerto Rico, to apply United States norms for hematocrit measure for the Puerto Rican population, too. As seen, however, in the results of our study there is a consistent difference of about 6 degrees lower in Puerto Rican population in almost every level on the scale, in general, and also within specific age groups. The question arises whether this is an indication of our female population having a much higher incidence of anemia or it can be attributed to physiological adaptation to geographical, socio-economic and cultural differences.

In 1945 Hurtado et al established the relationship between hematocrit and altitude in the Andes of Perú (9). Since it is known that on higher altitudes there is a low  $pO_2$  in the inspired air an increase in plasma Erythropoietin activity is found with its consequent compensatory polycitemia (8). Due to the geographical location of Puerto Rico most of our population lives near sea level or no altitudes not more than 2,500 feet above sea level, in which case polycythemia due to low  $pO_2$  in inspired air is not likely to be found.

Of greater importance however is the nutritional status of the Puerto Rican population. Fernández, N. A. et al (2, 3, 4) in several studies of nutrition of our population during the years 1963 to 1966 found that the diets of our Puerto Rican people were, although adequate, somewhat deficient in calories, proteins and iron. No significant differences were, however, found in the diet by socio-economic levels. Osifo, B. O. A. (1), on a similar study in Nigerian children suggested that the low hemoglobin levels he found were probably due to overhydration, with high plasma volumes

TABLE IV

## Hematocrit Level for Selected Percentiles for Puerto Rican Women by Age Groups

Percentiles	AGE GROUP			
	21 - 25 Years	26 - 30 Years	31 - 35 Years	36 - 40 Years
99.0	46.1	46.6	46.6	46.4
97.5	44.0	45.1	45.2	44.8
95.0	42.1	42.7	43.0	42.4
90.0	40.8	41.1	41.4	40.9
80.0	39.4	39.5	39.6	39.7
75.0	38.8	38.9	39.0	39.2
70.0	38.3	38.4	38.4	38.5
60.0	37.4	37.5	37.6	37.4
50.0	36.6	36.6	36.7	36.4
40.0	35.8	35.7	35.8	35.5
30.0	35.1	34.9	34.9	34.6
25.0	34.7	34.5	34.5	34.0
20.0	34.1	33.8	33.8	33.2
10.0	32.5	32.1	31.9	31.2
5.0	30.4	30.4	30.0	29.7
2.5	28.9	29.3	29.0	28.4
1.0	26.9	26.4	27.5	26.3
Mean	36.6	36.6	36.7	36.4

resulting from protein and calorie deficiencies and that this could be a case of physiological adaptation to low protein intake.

It is therefore possible that the low hematocrit in Puerto Rican women may not be indicating the anemic conditions, but can be attributed to eating habits.

It is important to note that the hematocrit level, 36.6 percent as an average of Puerto Rican women may be a concern of all when compared with about 6 point higher average in the United

States, but it is also important to look into the classification of Puerto Rican women as "anemic" by applying United States standards. There would be more than 50 percent of Puerto Rican women considered anemic (Table III, Graph I) if we consider 37 percent hematocrit level as the critical point according to United States norms. Probably it is advisable to undertake a more thorough and detailed study of hematocrit level among the population of Puerto Rico in general and establish specific standards for the popula-

TABLE V

Hematocrit Level for Selected Percentiles for United States Women by Age Group

Percentile	A G E G R O U P		
	18 - 24 Years	25 - 34 Years	35 - 44 Years
99.0	50.5	51.6	50.7
97.5	49.0	49.5	49.5
95.0	47.5	48.0	48.5
90.0	46.0	46.0	47.0
80.0	44.5	45.0	45.5
75.0	44.2	44.5	44.8
70.0	43.5	44.0	44.0
60.0	42.5	43.0	43.0
50.0	42.0	42.0	42.0
40.0	41.0	41.0	41.5
30.0	39.5	40.0	40.5
25.0	39.2	39.6	40.0
20.0	38.5	39.0	39.5
10.0	36.5	37.0	37.0
5.0	34.5	35.0	35.5
2.5	33.0	33.5	33.0
1.0	31.0	31.1	30.8
Mean	41.4	41.8	42.0

tion concerning the classification of anemic patients, using their other symptomatic conditions.

For the time being, however, one may use tentative hematocrit limits as follows: If we assume that the critical hematocrit level for anemic persons in the United States is 37 ml. percent and that the same proportion (8 percent to 10 percent from Table V) as the population of anemic women in United States exists in Puerto Rico, the critical hematocrit level equivalent for a Puerto Rican woman between age 21 - 40 would be considered about 31 or 32 ml.

percent; if we use the values of Table III or IV. Until a more detailed study is done for Puerto Rican population wherein the critical hematocrit level can be established in relation with other recognizable symptoms of anemia, this level (32 percent Hct.) may be used for classifying Puerto Rican women as anemic.

#### Acknowledgment

Appreciation is expressed to G. D. Searle and Co. for supplying Enovid.



## References

1. Bola O. A. Osifo: "The effect of diet in the hemoglobin and hematocrit value of some Nigerian village children". Br. J. Nutr. Vol. 24, 1970.
2. Fernández, N. A., Burgos, J. C., Robert, L. T., Asenjo, C. F.: "Nutritional status in Puerto Rican slum area". Amer. J. of Clin. Nutr. Vol. 21, No. 6, June 1968 pp.646-656.
3. Fernández, N. A., Burgos, J. C., Asenjo, C. F., Rosa, I.: "Nutritional survey of five rural Puerto Rican communities", Bol. Asoc. Méd. of P. R., Vol. 61 No. 2, February 1969.
4. Fernández, N. A., Burgos, J. C., Asenjo, C. F., Rosa, I.: "Nutritional status of the Puerto Rican population: Master Sample Survey". The Amer. J. of Clin. Nutr. 24: August 1971 - pp. 952-965.
5. Fuertes de la Haba, A., Bangdiwala, I., Pelegrina I.: "Success of Randomization in a controlled contraceptive Experiment", J. Reprod. Med., Vol. 11 No. 4, October 1973 (Series 11 No. 42)
6. Fuertes de la Haba, A., Bangdiwala, I., Roure, C.: "Effect of oral contraceptives on hematocrit level", Pending for publication.
7. National Center for Health Statistics Serie 11 No. 42, "Mean Blood hematocrit of adults United States - 1960-1962"
8. Scaro, J. L., Guidi, E. E.: "Relationship between plasur Erythropoietin activity and hematocrit ratio in high altitude residents".
9. Whittembury, J., Monge, C. C.: "High altitude, hematocrit, and age", Nature, Vol. 238, August 4, 1972.



Colleague...

# PITFALLS IN PRESCRIBING ADDITIONS FOR THE ELDERLY

Manuel N. Miranda, MD

**Abstract:** Elderly hyperopic patients usually require less plus power for distance, and their vision is usually reduced when they develop nuclear sclerosis. To maintain comfortable vision for near they need strong bifocal additions. A method to calculate the adequate reading addition is given.

**Abstracto:** Pacientes hiperópicos seniles usualmente necesitan menos potencia positiva para distancia y su visión usualmente se empeora para distancia cuando desarrollan esclerosis nuclear. Para mantener una visión cómoda para lectura necesitan adiciones fuertes. Se presenta un método para calcular la adición adecuada.

Not infrequently, I have had elderly patients who had recently been given a new prescription, complaining that they see better with their old glasses than with their new ones. On checking them, I found that most saw better with their new prescription for distance, but for reading, better with their old glasses. They feel more comfortable with their old glasses, since they can read better with them.

These elderly patients are usually hyper-

opes who have become less hyperopic because of an increase in the refractive power of the eye. The increase of power occurs in the nucleus of the lens, a development known as nuclear sclerosis. It is indicative of an early stage of senile cataract.

## Case Presentation

1. A retired male, 70, complained that his old glasses enabled him to see better than his new glasses. He had been given the following prescription:

O. D. + 1.00 - 0.50 x 90  
O. S. + 1.25 sphere  
add + 2.50

With this prescription he had 20/40 at distance in each eye, but only Jaeger 4 for reading. With his old glasses he was able to read Jaeger 1. His old prescription was

O. D. + 2.50 sphere  
O. S. + 2.75 sphere  
add + 2.50

2. A housewife, 68, had the same complaint. She had recently been given the following prescription:

O. D. + 0.75 + 0.50 x 180  
O. S. + 0.50 + 0.25 x 180  
add + 2.75

At distance she had 20/60 with the right eye, and 20/50 with the left eye; but at near, only Jaeger 5. With her old prescription:

---

*Del Departamento de Oftalmología, Escuela de Medicina, Universidad de Puerto Rico.*

*Presentado en la Reunión Anual de la Sección de Oftalmología de la Asociación Médica de Puerto Rico en el Hotel Palmas del Mar, Humacao, Puerto Rico, en julio 23 de 1977.*

*Favor de solicitar reproducciones a: Manuel N. Miranda, M. D., G. P. O. Box D, San Juan, Puerto Rico 00936.*

O. D. + 3.00 + 0.50 x 180  
O. S. + 2.50 sphere  
add + 2.50

she was able to read Jaeger 1.

### Comment

The refractionist failed to recognize the special bifocal needs of these two patients. (They actually were subnormal vision cases, and should have been handled as such.)

The individual needs of the patient should be determined from his history, habits and purposes and the bifocal add then determined by actual measurement. A good rule of thumb to select the first trial reading lens is to apply the following formula: (1)

$$\text{Add} = \frac{2}{\text{VA}} - 0.50$$

This lens would be sufficient in most cases.

If the visual acuity of one eye is different from that of the other, the better visual acuity should be taken.

According to this rule the first patient should have been given an addition of + 3.50 found by applying the formula  $\frac{2}{\text{VA}} - 0.50$

$$\begin{aligned}\text{Add} &= \frac{2}{20/40} - 0.50 \\ &= \frac{2}{0.5} - 0.50 \\ &= 4.00 - 0.50 \\ &= + 3.50\end{aligned}$$

The prescription should have been

O. D. + 1.00 - 0.50 x 90  
O. S. + 1.25 sphere  
add + 3.50

His old glasses had enough plus power for

reading comfortably (O. D. + 5.00 sphere; O. S. + 5.25 sphere) and that is why he was able to read Jaeger 1 with his old glasses.

The second patient should have been given an addition of + 4.50 found by applying the formula  $\frac{2}{\text{VA}} - 0.50$  in the left eye, the eye with best visual acuity.

$$\text{Add} = \frac{2}{20/50} - 0.50$$

$$= \frac{2 \times 50}{20} - 0.50$$

$$= 5.00 - 0.50$$

$$= + 4.50$$

The prescription should have been

O. D. + 0.75 + 0.50 x 180  
O. S. + 0.50 + 0.25 x 180  
add + 4.50

Her old glasses met the criteria of the formula for reading (O. D. + 5.50 + 0.50 x 180; O. S. + 5.00 sphere) and that is why she was able to read Jaeger 1 with her old glasses.

### Conclusion

It is important to be aware of the bifocal addition needs for elderly patients who have developed nuclear sclerosis.

For those who do not like to use formulas as a guide, a good method to follow is to take the first number of the visual acuity fraction denominator for a distance of twenty feet and subtract 0.50 to get the bifocal add for these patients.

### Reference

1. Boeder, P.: Personal communication, April, 1977.





- A. 90 year old male patient who presented with complete atrio-ventricular heart block.

The chest X-ray is shown above.


The most probable diagnosis is:

1. Calcified ventricular aneurysm.
2. Pericardial cyst.
3. Calcified mitral valve annulus.
4. Atrial Myxoma.



- B. This 90 year old male with a calcified mitral valve annulus presented to the Hospital with syncope and complete A-V block. Electrophysiologic evaluation revealed block within the His-Purkinje system. Please note the inverted J type calcification in the mitral area (arrows). Compare this type of mitral annular calcification with the calcification seen in ventricular aneurysm (case report published last month). The incidence of complete A-V block in patients with mitral annular calcification has been reported to be about 4-5 percent.

Migdalia González, MD  
Julio E. Pérez, MD  
Guillermo Cintrón, MD  
Esteban Linares, MD  
Edgardo Hernández, MD  
Juan M. Aranda, MD  
Cardiology Service, Veterans Adm. Hospital,  
San Juan, Puerto Rico



## Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx. 1,000 tons)

**Most Widely Prescribed**—Antivert is the most widely prescribed agent for the management of vertigo\* associated with seasickness affecting the vestibular system such as Menière's disease, labyrinthitis, and vestibular neuronitis.

**Relief of Nausea and Vomiting**—Antivert/25 can relieve the nausea and vomiting often associated with vertigo.\*

**Dosage for Vertigo\***—The usual adult dosage for Antivert/25 is one tablet t.i.d.

### BRIEF SUMMARY OF PRESCRIBING INFORMATION

**INDICATIONS.** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

**Effective:** Management of nausea and vomiting and dizziness associated with seasickness.

**Possibly Effective:** Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

**CONTRAINDICATIONS.** Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg/kg/day in rabbits and 10 mg/kg/day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

**WARNINGS.** Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.


**Usage in Children:** Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

**Usage in Pregnancy:** See "Contraindications."

**ADVERSE REACTIONS.** Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

**ROERIG**   
A division of Pfizer Pharmaceuticals  
New York, New York 10017

**Antivert<sup>®</sup>/25**   
(meclizine HCl) 25 mg. Tablets  
**for vertigo\***



# TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE **DYAZIDE®**

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

**\* Warning**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**\* Indications:** When the combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium sparing action of triamterene is warranted. (See Box Warning.) Routine use of diuretics in healthy pregnant women is inappropriate; they are indicated in pregnancy only when edema is due to pathological causes.

**Contraindications:** Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K<sup>+</sup> levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K<sup>+</sup> intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids).

Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K<sup>+</sup> frequently; both can cause K<sup>+</sup> retention and elevated serum K<sup>+</sup>. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis.

'Dyazide' interferes with fluorescent measurement of quinidine.

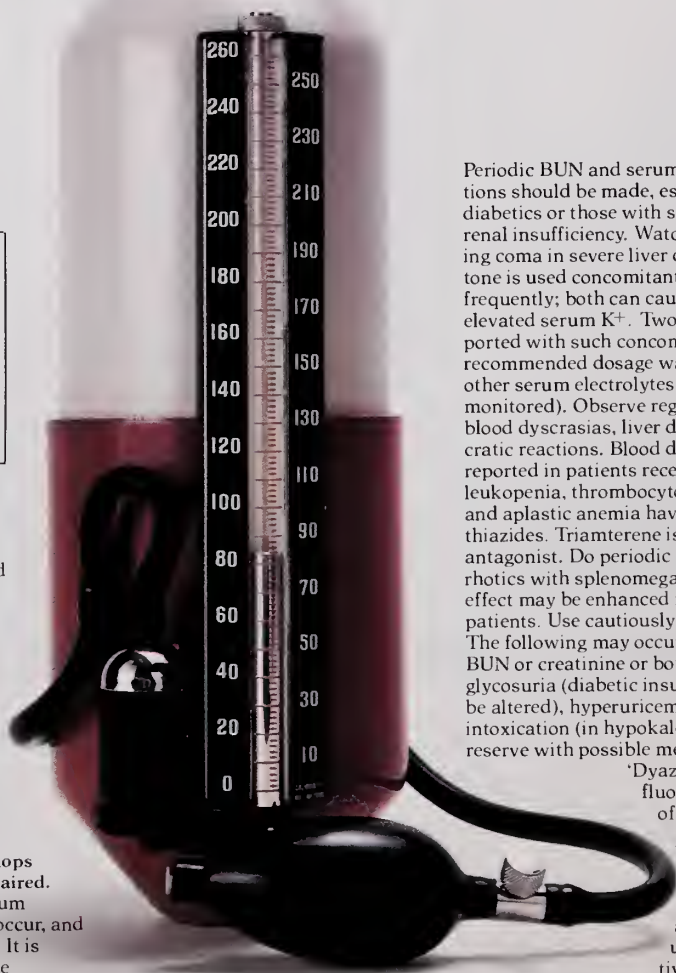
**Adverse Reactions:**

Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

SK&F CO., Carolina, P.R. 00630

**FOR LONG-TERM CONTROL  
OF HYPERTENSION\*  
SERUM K<sup>+</sup> AND BUN SHOULD  
BE CHECKED PERIODICALLY.  
(SEE WARNINGS SECTION.)**



**SK&F CO.**  
a SmithKline company

**ABSTRACTOS: TRABAJOS A PRESENTARSE EN  
LA ASAMBLEA ANUAL - AMPR - NOV. 7 - 12, 1977  
SALON DE CONVENCIONES - CONDADO**

**NOSOCOMIAL INFECTIONS SURVEILLANCE**

*Livia M. Bermúdez, MSIV, Ramón H. Bermúdez, MD, FACP and Marta Figueroa, MSN, VA Hospital and University of Puerto Rico School of Medicine, San Juan, Puerto Rico.*

Nosocomial infections are a serious problem in terms of cost, morbidity and mortality. During the past three years (1974-1976) the Infection Control Nurse assisted by the Microbiology Section has been conducting surveillance of hospital-acquired infections at the San Juan VA Hospital by reviewing medical records and bacteriological laboratory reports. The attack rate has been 7 percent. The prevalence of nosocomial infections has been greatest during the early and middle part of the year. The urinary tract has been the most frequent infection site (275 cases/year). The most common pathogens isolated have been gram-negative bacilli and *Staphylococcus aureus*. Nosocomial bacteremia have been more frequent in the Medical Service. Antibiotic auditing has revealed that the most common antibiotics used were the penicillins, cephalosporins and gentamycin. The most frequent isolates in nosocomial bacteremia were: *Klebsiella-Enterobacter* 18 percent, *E. coli* 16 percent, *Proteus* spp. 13 percent, *Pseudomonas* spp. 12 percent and *Staphylococcus aureus* 23 percent. Other strains of gram-negative bacilli were recovered in 18 percent of bacteremic cases. At our institution gram-negative bacilli are the most common pathogens causing nosocomial infections, but the number

of cases due to staphylococci is increasing. There is a great need to perform surveillance of nosocomial infections and to analyze susceptibility patterns to antibiotics in order to help the clinician manage serious hospital-acquired infections.

**HEMODYNAMIC AND ANGIOGRAPHIC OBSERVATION IN PATIENTS SURVIVING VENTRICULAR ANEURYSMECTOMY**

*Migdalia González, MD, Esteban Linares, MD, Edgardo Hernández, MD, Guillermo Cintrón, MD and Juan M. Aranda, MD.*

Late clinical and hemodynamic evaluations in 18 patients with ventricular aneurysmectomy and aorta-coronary bypass are presented. Ten patients had significant obstructive lesions in two major vessels (55 percent), and 6 had extensive three vessel disease (33 percent). In 13 patients, 21 aorta-coronary saphenous bypass grafts were performed in addition to aneurysmectomy. The operative mortality rate was 11 percent. One patient died suddenly 5 months after the operation (one year mortality rate 17 percent). The 15 surviving patients have been followed up for 12 to 41 months (average 24 months). Clinical results were considered excellent in 2 patients who have been asymptomatic (Class I, N.Y.H.A.). Nine others were considered to have good clinical results (Class II). Five patients have continued to have congestive heart failure and angina on minimal effort (Class III or IV). Six of the 11 patients considered to have excellent or good results underwent postoperati-



ve hemodynamic studies 6 to 34 months after the operation. A significant increase in cardiac index was documented in all 6 patients. Paradoxical movement was not detected in any of the postoperative ventriculograms. Five of the seven venous grafts inserted were patent. Elevated left ventricular end-diastolic pressure (LVEDP), low cardiac index, and a persistent dyskinetic area in the left ventricle were found in 2 patients considered to have poor clinical results. Clinical and hemodynamic evaluations have shown a significant improvement in most patients surviving ventricular aneurysmectomy. However, postoperative systemic embolism, myocardial infarction, and mitral regurgitation in previously prolapsed mitral valve leaflets account for progressive disability and limited activity after a successful operation.

#### PROTECCION CONTRA TETANO EN PUERTO RICO

*Héctor F. Gorbea, MD, Rosa Llubes, MT and Carlos H. Ramírez Ronda, MD, FACP. Departamentos de Investigación y Medicina, Hospital de Veteranos y Escuela de Medicina, Universidad de Puerto Rico, San Juan, Puerto Rico.*

El tétano es un problema en Puerto Rico siendo 13 veces más frecuente que en los EE. UU. Se diseñó un estudio prospectivo para determinar el nivel de protección en contra de tétano en diferentes grupos poblacionales de la isla. Se estudiaron 438 sujetos, 236 varones, 172 mujeres y 30 recién nacidos. El grupo incluía 138 veteranos, 136 no veteranos, 72 médicos (Internos y Residentes), 66 mujeres embarazadas y 30 recién nacidos. Los niveles de antitoxina de tétano (ATT) se midieron por hemaglutinación. La protección ATT se definió como un nivel  $\geq 0.01$  unidades antitoxina/ml. No se encontró protección en el 9.3 por ciento de los varones y en el 7.5 por ciento de las mujeres; todos los recién nacidos tenían

protección al igual que las mujeres embarazadas. El nivel de protección disminuyó progresivamente con la edad. Se encontraron 125 sujetos de 50 años de edad o más, 27 (22 por ciento) no tenían protección. De los 313 sujetos menores de 50 años solamente el 2 por ciento no tenía protección. En el estudio de la comunidad, los niveles más bajos de protección se encontraron en mujeres de 50 años o más de edad, mientras que en los otros grupos los niveles más bajos se encontraron en los varones. Todos los recién nacidos y sus madres tenían protección, pero el nivel ATT en la sangre umbilical fue el 12 por ciento del nivel en sangre materna. En Puerto Rico nuestra población joven está protegida contra el tétano, reflejando los esfuerzos de inmunización de las Agencias de Salud, pero una porción significativa de nuestra población de 50 años o más (22 por ciento) está sin protección. Recomendamos la institución de un programa de vacunación y campaña de educación en salud dirigida a nuestra población de 50 años o más. Una vez la serie primaria se haya completado, endosamos fuertemente el uso del toxoide de tétano y difteria (Td) cada 10 años.

#### ESTUDIO LONGITUDINAL DE LA FLORA FARINGEAL DE INTERNOS Y RESIDENTES (I y R): UN ESTUDIO PROSPECTIVO.

*Z. Fuxench-López, MD y C. H. Ramírez Ronda, MD, FACP. Departamentos de Investigación y Medicina, Hospital de Veteranos y Escuela de Medicina de la Universidad de Puerto Rico, San Juan, Puerto Rico.*

La colonización por bacilos gram-negativos (BGN) de la faringe de personas normales es alrededor del 2 al 9 por ciento, mientras que en el alcohólico ambulatorio es alrededor del 64 por ciento. Un número significativo de pacientes admitidos al hospital se colonizan por BGN y todos los pacientes seriamente enfermos admitidos a intensivos se colonizan con BGN



en 72 horas de hospitalización. La flora predominante en el hospital son BGN. Para ver los efectos del ambiente del hospital en la colonización faríngea de médicos, un grupo de I y R saludables fue estudiado prospectivamente y longitudinalmente. Cultivos cuantitizados seriados se tomaron en un período de 12 meses. La identificación se llevó a cabo por métodos bacteriológicos conocidos. Uno o más BGN fue aislado en el cultivo inicial de 16 por ciento (14/89) de los I y R. 4.4 por ciento de los sujetos tenía más de 1 BGN. La tasa de colonización fue alta ( $< 10$  UFC/ml) en 11/14. Dos sujetos tenían patógenos gram positivos en números altos. En el estudio longitudinal de 22 I y R, el número de cultivos positivos para BGN fue 13.6 por ciento (3/22). En cultivos semanales o cada dos semanas, la colonización no persistió excepto en 2 sujetos. Los organismos más frecuentemente aislados fueron *Klebsiella pneumoniae* 35 por ciento, *Escherichia coli*, 14 por ciento, *Enterobacter aerogenes* 14 por ciento y *Enterobacter cloacae*, *Citrobacter diversus*, *Enterobacter agglomerans*, *Klebsiella ozaenae* y *Serratia liquifaciens* 7 por ciento cada uno. Los datos sugieren que la colonización faríngea de I y R es más alta que la de pacientes ambulatorios, pero esta colonización es transitoria. La colonización es en números altos reflejando exposición continua, y es por los mismos organismos que se encuentran en el ambiente del hospital.

#### MUCORMYCOSIS OSTEOMYELITIS IN A CONTROLLED DIABETIC PATIENT.

David E. Martínez, MD, Rodolfo Alejandro, MD, Jeanette Hoyer, DDS, Ramón Cabañas, MD, Carlos H. Ramírez Ronda, MD, FACP. University of Puerto Rico School of Medicine and Dentistry, San Juan, Puerto Rico.

Mucormycosis is a fungal disease that in its rhinocerebral form is usually seen in patients with uncontrolled diabetes mellitus

and ketoacidosis. We present an unusual case of a 65 years old woman with adult onset diabetes that presented with localized osteomyelitis of the maxillary bone secondary to mucormycosis. On April 1976 she developed a painful swelling of the left side of the face with suppuration and bleeding from the nasal region; was diagnosed as sinusitis and treated with antibiotics. On September 1976 due to the persistence of pain and suppuration, an exploration of the left maxillary bone was performed showing osteomyelitis. On October 1976 she was admitted to the UDH where further surgery was performed with removal of all tissue and necrotic bone, the pathological specimen studied was diagnostic of mucormycosis. The patient's clinical presentation was a benign one. She was afebrile with normal vital signs, normal hemogram, normal chemistries and a blood sugar of 140 mg percent. Sinus films revealed mucosal thickening of both maxillary sinuses and bony changes on the left. The patient was started on IV Amphotericin B and received a total dose of 2 gms over a period of 83 days. During therapy she developed an anemia, mild azothemia and electrolyte changes. Brain scan and EEG were normal. On discharge, sinus x-rays showed muco-periorbital thickening of the left maxillary sinus and no evidence of osteomyelitis but the patient continued with pain. The case is presented to aware us that chronic or recurrent sinusitis in a diabetic can be the first sign of rhinocerebral mucormycosis and that early treatment can cure the infection.

#### LEFT VENTRICULAR ANEURYSMECTOMY AND VENTRICULAR SEPTAL DEFECT REPAIR FIVE WEEKS AFTER ACUTE MYOCARDIAL INFARCTION.

Julio E. Pérez, MD, Edgardo Hernández, MD, Esteban Linares, MD, et al. Veterans Administration Hospital.

A 67-year old male patient was referred to our institution after sustaining an acute myocardial infarction which was complicated two weeks later by left ventricular failure and ventricular septal rupture. A right heart catheterization performed upon admission documented the septal rupture, and estimated the QP/QS in 1.3:1. Mild elevation of the PCWP to 14 mm Hg was noted. The hospital course was characterized by progressive left ventricular failure and intermittent ventricular arrhythmias. Cardiac catheterization was performed five weeks after myocardial infarction and revealed a large left ventricular aneurysm that occupied the anteroapical, apex and inferoapical segments. The left anterior descending artery was 100 percent obstructed near its origin without distal runoff and the right coronary artery showed a 70 percent lesion in its middle third. Sodium nitroprusside was given for the next two days and the patient underwent surgery where aneurysmectomy and ventricular septal repair were carried out. The postoperative course was complicated by pneumonia and transitory personality changes. The patient was discharged five weeks after surgery otherwise asymptomatic.

Acquired ventricular septal defect and its associated lesions can be repaired safely after an initial stabilization period.

## POST TRAUMATIC THORACIC AORTIC ANEURYSMS

*E. A. Defendini, MD and J. C. Medina. School of Medicine UPR*

Sudden deceleration type of injuries such as occur in automobile accidents may lead to traumatic rupture of the thoracic aorta. These lesions if not recognized promptly may lead to death in a short period of time but some may go on to form thoracic aneurysms which will

eventually rupture. The mechanism of aortic injury, diagnosis and treatment together with the discussion of two cases of thoracic aneurysms treated successfully will be presented.

## FUNCTIONAL SIGNIFICANCE OF ELECTROCARDIOGRAPHIC CHANGES AFTER LEFT VENTRICULAR ANEURYSMECTOMY

*Juan M. Aranda, MD, Esteban Linares, MD, Edgardo Hernández, MD and Guillermo Cintrón, MD. Veterans Administration Hospital*

Electrocardiographic (ECG) changes after left ventricular aneurysmectomy were analyzed in 20 patients; thirteen of whom had additional aorto-coronary saphenous vein bypass surgery. ECG changes were correlated with post-operative clinical and hemodynamic results. Out of 14 patients (Group I) who showed hemodynamic and/or clinical improvement, 8 had decrease of chronic ST segment elevation that was associated in 5 with loss of pathologic Q waves. In the remaining 6 patients (Group II) who showed no hemodynamic and/or clinical improvement as well as in 6 patients in Group I, chronic ST segment elevation persisted or increased and in some, loss of pathologic Q waves developed after surgery. The study suggests that loss of pathologic Q waves and/or decrease of chronic ST segment elevation in patients who undergo a left ventricular aneurysmectomy with aorto-coronary saphenous vein bypass surgery, may reflect postoperative clinical, hemodynamic and angiographic improvement. On the other hand, failure of these ECG changes to occur or conversely, increased ST segment elevation and/or appearance of new Q waves may have no predictive value. The mechanisms for these ECG changes are discussed.

## OPEN HEART SURGERY IN SMALL COMMUNITIES. FEASIBLE OR NOT?

*J. O. Just Viera, MD, A. Lui, MD, F. Bunker, MD and B. Sou, MD. Mercy Hospital, Benton Harbor, Michigan 49022.*

Where should future resources be allocated to meet the increasing demand for myocardial revascularization? Population rural migration, energy and urban crises will require increased delivery of specialized cardiac services in small communities. This paper aims to stimulate discussion and provide information useful in health planning.

The results of solo practice in open heart surgery at Mercy Hospital, Benton Harbor, Michigan, a 177 bed community hospital will be presented. Coronary artery bypass (majority double or triple) and ventricular aneurysmectomy constituted 83 percent of 191 procedures. Valvular and congenital surgery comprised the rest. Mortality was 5 percent, and no deaths occurred since April, 1976. Patients were classified according to ventricular function.

Open heart surgery is possible and provides striking benefits to medical care in small communities. The following requisites are essential: prompt identification and solution of system failures; imaginative and varied use of specialized personnel; continuous training and proficiency testing; physician education; close cooperation with general surgeons; strict adherence to both cost control and quality standards; and total administrative and community commitment to the program. Priorities, potential problems and rewards are different from the academic setting.

## HIPERBILIRUBINEMIA EN PACIENTES CON INFARTO DEL MIOCARDIO

*José M. Martín Trilla, MD y M. Martínez Maldonado, MD. Del Servicio de Medicina y Fisiología, Hospital de Veteranos.*

Bilirubina es el producto del catabolismo de las hemoproteínas. Elevación de éstas se ha descrito en un sinnúmero de condiciones en ausencia de hemólisis y enfermedad hepatobiliar. De éstas, la más frecuente fue enfermedad cardíaca. Se revisaron 24 pacientes con infarto agudo del miocardio con criterios enzimáticos y electrocardiográficos. Se eliminaron todos aquellos que tuvieron evidencia de infección, embolia pulmonar, enfermedad hepática crónica, insuficiencia cardíaca. Veinticuatro (70 por ciento) de éstos presentaron elevaciones de bilirubina de 1.1–3.1mg por ciento con un promedio de 1.75 mg por ciento en los días 1 al 3. Después éstos regresaron a valores normales. De estos 24, 4 permanecieron con elevación al ser dados de alta, lo que sugiere otra patología envuelta. Se comparó con 22 pacientes admitidos con dolor de pecho pero sin infarto y solamente 3 de éstos presentaron elevaciones de bilirubina: uno con enfermedad arteriosclerótica y uno debido a fenotiazinas. Las posibilidades fisiopatológicas se discutirán.

## PROGRESSION OF CORONARY ARTERY DISEASE AFTER AORTO-CORONARY SAPHENOUS VEIN BYPASS

*Julio E. Pérez, MD, Guillermo Cintrón, MD, Esteban Linares, MD, Edgardo Hernández, MD and Juan M. Aranda, MD. Veterans Administration Hospital.*

Progression of coronary artery disease after aorto-coronary saphenous vein bypass grafting was studied in 79 of 180 consecutive patients operated on at the Veterans Administration Hospital from January 1972 to July 1975. The mean interval after the surgical procedure was 13 months. Thirty three patients (42 percent) had excellent or good results (Class I-II NYHA) and were restudied to evaluate the status of the



grafts or because recurrence of mild angina on exertion. Forty six patients (58 percent) were evaluated because persistent or recurrent angina on minimal effort (Class III-IV).

In the 79 patients studied, 157 aorto-coronary bypass grafts with reversed saphenous veins were performed, 78 arteries were not grafted. Progression of obstruction and appearance of new lesions in the distal segment of the coronary arteries occurred in 3.6 percent and 12 percent respectively in ungrafted arteries. There were no significant differences in the appearance of new lesions in grafted and ungrafted arteries. Progression of obstruction was found in 44 percent of 99 coronary arteries with patent grafts and 22 percent in coronary arteries with occluded grafts; strictures at the anastomotic site were found in only 2 cases.

Contrary to previous reports, progression of obstructive lesions is dependent on the patency of the grafts and appears to be secondary to altered coronary hemodynamics. The appearance of new lesions distal to the site of anastomosis is not different in grafted or ungrafted arteries and probably represents natural progression of the atherosclerotic process.

## MANEJO CONSERVATIVO DE TRAUMA ESPLENICO

*Pedro J. Rosselló, MD y Angelo E. Eraklis, MD. Del Depto. de Cirugía, Escuela de Medicina UPR y Harvard Medical School*

Recientemente se ha establecido que la esplenectomía en el grupo pediátrico conlleva un riesgo aumentado de sepsis y mortalidad. Debido a esto durante los últimos meses años en el Children's Hospital Medical Center, Boston, se ha seguido un regimen conservador en el tratamiento lesiones traumáticas al bazo. Durante este período 24 casos laceraciones

o ruptura de bazo fueron tratados sin esplenectomía. Cuatro fueron documentados durante laparotomía: a tres de éstos se les reparó las laceraciones y a uno se le practicó esplenectomía parcial. Ninguno tuvo complicaciones secundarias a estos procedimientos. En los veinte casos restantes, no se exploró al paciente. El diagnóstico de ruptura luego del trauma como se confirmó mediante un scintigrama de bazo o un arteriograma. Se admitieron al servicio quirúrgico y se les tuvo bajo cuidadosa observación de signos vitales, hematocrito, y presión venosa central. En algunos casos hubo que administrar transfusiones hasta máximo de 50 por ciento del volumen sanguíneo. Ninguno requirió cirugía, agudamente o durante el período de seguimiento. Se le dio seguimiento con scintigramos seriados a trece de veinte pacientes y en ninguno hubo evidencia de agrandamiento del defecto inicial; tres demostraron resolución completa, ocho una mejoría del defecto y dos se mantuvieron estables. Clínicamente no se demostraron complicaciones algunas después de darse de alta.

## INCIDENCIA DE FISTULA FARINGOCUTANEA EN LARINGUECTOMIZADOS

*Juan Trinidad Pinedo, MD. Departamento de Otorrinolaringología, UPR.*

La complicación más común en pacientes laringuectomizados la constituye la fístula faringocutánea, que transforma un post-operatorio difícil en tormentoso, con un incremento en la morbilidad y estancia hospitalaria.

El propósito de este trabajo es doble; en primer lugar presentan la incidencia de fístula faringocutánea en aquellos pacientes laringuectomizados durante el período 1967-1974 en los Hospitales Universitario, Municipal y Oncológico, que resultó ser del 48 por ciento que está comprendido entre el 20 por ciento y 70

por ciento que cita la literatura, así como buscar una relación de esta frecuencia con los distintos factores desencadenantes.

En la segunda parte, se describe un método de estudio del post-operatorio mediante esofagogramas seriados, que permite disminuir la incidencia en la presentación de fístula faringocutánea al 16 por ciento, en los pacientes que sufrieron laringuectomía en el transcurso entre los años 1975-1977.

Concluyendo, el estudio seriado con esofagogramas permite: 1. disminuir la incidencia de F. F., 2. predecir la Fístula, 3. Demostrarla. 4. seguir la cicatrización faringoesofágica, 5. conocer el momento de iniciar la alimentación oral, 6. detección de persistencia tumoral.

## THE ROLE OF THE OTOLARYNGOLOGIST IN THE EARLY DIAGNOSIS OF CEREBELLOPONTINE ANGLE TUMORS

*Alexis O. Fernández, MD*

Tumors of the cerebellopontine angle are indeed rare lesions. Nevertheless, failure to make the correct diagnosis can have disastrous consequences. It is imperative that these lesions be diagnosed as early as possible so as to prevent the serious consequences of a delayed diagnosis, such as complete hearing loss and facial paralysis, which may ensue as either the result of the tumor itself or the surgical intervention required.

A high index of suspicion is, of course, mandatory in any patient presenting with a unilateral, sensori-neural hearing loss of obscure etiology. This is usually accompanied by tinnitus and a discrimination loss greater than that one would normally expect with the hearing loss as seen in the pure tone audiogram of the given patient.

A diagnosis will usually require a careful history and physical examination; full audio-

metric evaluation including pure tone, air, bone and speech audiograms; radiologic evaluation of the internal acoustic meati, including tomography of the temporal bones and perhaps a pantopaque study.

More recently, the advent of tympanometry as an office procedure has acquired tremendous importance in the diagnosis of these lesions. An absent or rapidly decaying stapedius reflex is probably the single, most reliable measurable parameter observable in angle lesions.

## CRYOGENIC STEREOTAXIC HYPOPHYSECTOMY

*René Cardona Campos, MD, FACS. Neurosurgery Service UPR*

Two cryogenic stereotaxic hypophysectomies have been performed in Puerto Rico, both by the author at the VA Hospital in San Juan. Both patients had carcinoma of the breast with metastases. The technique of cryogenic hypophysectomy is described as well as the role of Estrogen Receptor Assay in carcinoma of the breast.

## BLEEDING VARICES — NEW HOPE

*Enrique Márquez and Elihu Ledesma, MD*

The senior author's personal experience with 15 consecutive cases of portal hypertension of different etiology. All cases had bled previously. They were treated surgically with the new Distal Splenorenal Shunt devised by Warren. All patients survived and there was minimal morbidity. It is essential that patient have high quality mesenteric and renal angiographic studies and be free of ascites.

## THE USE OF PENILE PROSTHESIS IN CASES OF MALE IMPOTENCE

*Carlos C. Maestre, MD and José I. Gerena, MD*

The implantation of penile prosthesis for the treatment of male impotence have gained progressive importance. Advances in design and research with silicone materials offer the patient with organic impotence an opportunity for better social and psychological adaptation.

We explain the kind of prosthetic devices, surgical techniques, possible complications and our results with the first two cases in Puerto Rico in whom the "Scott" dynamic, hydraulic prosthesis was implanted.

condition is not known it is characterized by multiple immunologic alterations. The beneficial effects of Azathioprine in the course of SLE are well known. This study analyzes the effects of Azathioprine treatment in the course of SLE patients.

Forty four patients were included in the study. There were 37 females and 7 males. The age group was from 9 to 67 years. Thirty patients are still alive, of whom 25 are females and 5 are males. Fourteen patients died of whom 12 were females and 2 males. Twelve patients developed secondary effects such as hematologic alterations, infections and one patient developed liver toxicity. Of the 33 21 improved. At present 4 of these are in complete remission. Twelve patients failed to improve, of these, 3 died.

## PHEOCHROMOCYTOMA OF THE URINARY BLADDER: CASE REPORT AND REVIEW OF LITERATURE

*Andrés Acosta, MD, FACS, Francisco L. Burgos, MD, Jesús M. Vázquez, MD. San Juan Veterans Administration Hospital*

An interesting case of Paroxysmal post micturitional hypertension secondary to a pheochromocytoma of the bladder wall is presented. Light and Electron Microscopy material are presented and the literature on the subject is reviewed.

## APLICACION DEL GALIO 67 EN LA LOCALIZACION DE ENFERMEDADES INFLAMATORIAS

*Aldo E. Lanaro, MD, y Justo M. Caamaño, MD. División de Medicina Nuclear Escuela de Medicina UPR y Centro para Estudios Energéticos y Ambientales de la UPR.*

El Galio 67 fue introducido en Medicina Nuclear para localizar tumores. Accidentalmente se notó la captación de ese isótopo por abscesos o procesos infecciosos agudos o crónicos.

En el laboratorio del Centro para Estudios Energéticos y Ambientales (CEEAA) se comenzó en 1975 a usar este material para localizar procesos inflamatorios con resultados muy satisfactorios.

Se presentan características físicas del Galio 67. Dosis 3 mCi. Los estudios se hacen en Cámara o en Gamágrafo doble. Se presentan resultados de una serie de ejemplos de casos estudiados con este método. Imágenes obtenidas

## AZATHIOPRINE IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

*Esther N. González Parés, MD and Ivelisse Lebrón Nazario, MD. Rheumatology Section, Department of Medicine.*

Systemic Lupus Erythematosus (SLE) is a multiple system disease with an unpredictable cause. Although the etiology of this



y verificación posterior del diagnóstico. Se discute la ventaja del método por lo atraumático y localizante. Su utilidad en casos de procesos en tórax, abdomen o endocraneanos.

Mecanismo de fijación especialmente en granulocitos complementada por la mayor vascularización. Diferenciación de procesos tumorales de los infecciosos por la diferencia en el tiempo de aparición de las imágenes.

### ROLE OF PRECIPITATING ANTI-DNA ANTIBODIES IN THE NEPHRITIS OF SYSTEMIC LUPUS ERYTHEMATOSUS

*Julio E. Lergier Saliva, MD, Esther N. González Parés, MD and Alba S. Puente, MD. Centro Reumatológico de PR.*

Previous studies from our laboratory have demonstrated a significant correlation in patients with Systemic Lupus Erythematosus (SLE) between renal prognosis and survival and both the quantity of antinative deoxyribonucleic acid antibodies (n-DNA Ab) and the antigen binding avidity quality of n-DNA Ab. To clarify the role of precipitating (PPT) versus non-precipitating AB (NPPT) we compared PPT, NPPT and total n-DNA Ab in three (3) patients with SLE with diffuse proliferative glomerulonephritis (DPGN) who died with three (3) patients with SLE and focal proliferative glomerulonephritis (FGN) who did not show progression of disease and survived. All patients had high amounts of n-DNA Ab by the standard radio-immunoassay ( $>10$   $\mu$ gm. DNA/ml serum). Mean percentage of PPT Ab (PPT/total X 100) in the DPGN group was 80.6 percent as compared to only 48.6 percent in the FGN group. The preliminary finding of relatively higher amounts of PPT n-DNA Ab in SLE patients with severe renal disease and worse prognosis suggests a qualitative effect of increased pathogenicity of PPT Ab mediated possibly by enhanced tissue

deposition of DNA-anti DNA complexes and may provide an additional method for attempting to separate SLE patients into subgroups with differing outcomes.

### PEPTIC GASTRIC OUTLET OBSTRUCTION RESPONSIVE TO CIMETIDINE

*Angel Olazábal, MD and Pedro H. García-Pont, MD. Veterans Administration Hospital, Medical Service.*

Gastric outlet obstruction may complicate peptic ulcer disease. Medical therapy is frequently unsuccessful and gastric surgery is then required. We report the first patient with gastric outlet obstruction from severe peptic duodenal ulcer disease treated with intravenous cimetidine, a new potent inhibitor of gastric acid secretion.

A.A., a 31 year old male, was hospitalized for evaluation of early satiety, postprandial vomiting, intermittent epigastric pains, and twenty pound weight loss over the previous six months. Admission examination was unremarkable except for sinus bradycardia and an abdominal succussion splash. Radiographic series showed delayed gastric emptying. Esophagogastroduodenoscopy revealed a large duodenal ulcer with severe inflammation of the surrounding mucosa and narrowing of the duodenal lumen.

Nasogastric suction for fourteen days did not relieve the obstruction as documented by serial saline load tests. Intravenous cimetidine in a dose of 300 mg every six hours was then begun. Three days after initiation of cimetidine treatment gastric emptying had improved, and seven days later emptying had normalized.

Cimetidine has been continued orally in the same dosage and one month following discharge from the hospital the patient remained asymptomatic, eating a regular diet. Esophago-

gastroduodenoscopy revealed mild duodenitis without ulceration and narrowing of the duodenal lumen.

We conclude cimetidine improved the peptic duodenal inflammation and normalized the gastric emptying in this patient.

## NIVELES DE PROTECCION EN CONTRA DE DIFTERIA EN PUERTO RICO

*Rosa Lluberes, MT, Héctor Gorbea, MD y Carlos Pérez, MS II y C. H. Ramírez Ronda, MD, FACP. Departamentos de Investigación y Medicina, Hospital de Veteranos y Escuela de Medicina de la Universidad de Puerto Rico, San Juan, Puerto Rico*

La difteria es una enfermedad rara en Puerto Rico en la actualidad. Los casos clínicos son muy pocos reflejando un nivel de protección adecuado y/o colonización baja. Para determinar cuantitativamente los niveles de protección contra la difteria, se diseñó un estudio prospectivo en diferentes grupos poblacionales. Se estudiaron 462 sujetos, 149 veteranos, 141 no veteranos, 77 médicos (internos y residentes) 66 mujeres embarazadas y 29 bebés recién nacidos. Los niveles de antitoxina de difteria (ATD) se midieron por hemaglutinación indirecta. La protección de ATD se definió como un nivel  $\geq 0.01$  unidades de antitoxina por ml. El nivel de protección fue de 80 por ciento en los veteranos, 85 por ciento en los no veteranos, el 94 por ciento en los internos y residentes, el 95 por ciento en las mujeres embarazadas y el 62 por ciento en los recién nacidos. El nivel de protección disminuye con la edad del grupo estudiado, siendo 94 por ciento en pacientes de menos de 40 años y 76 por ciento en pacientes mayores de 40 años. El nivel de protección pasiva de ATD en los recién nacidos refleja, un nivel promedio de ATD en las mujeres embarazadas por debajo de niveles obtenidos en ATT. En Puerto Rico la población joven está protegida, más los niveles promedios de

protección de ATD son menores que los niveles de ATT. Esto refleja las prácticas de inmunización en niños con toxoide combinado de difteria, tétanos y tos ferina, sin recibir después de la edad escolar refuerzos de toxoide de difteria, mientras que el toxoide de tétano se recibe más frecuentemente. Los datos apuntan y reenfatizan la necesidad de vacunación de nuestra población adulta con toxoide tétano-difteria (Td) y de recomendar el uso del toxoide Td como refuerzo en vez del toxoide de tétano solamente.

## PLATELET DYSFUNCTION IN OPHTHALMIC ALBINISM

*Jean Fradera, BSMT, José J. Corcino, MD and Margarita Costas, MD*

Ophthalmic albinism is, in our experience, invariably associated with a platelet disorder and a mild bleeding diathesis. We have thus far evaluated six subjects with this syndrome. All the patients had a history of easy bruisability and some of them had profuse bleeding after molar extractions. They all had a prolonged bleeding time of over 15 minutes (normal 3-8) using the modified Ivy technic and platelet aggregation studies were compatible with Storage Pool disease. The different patterns obtained in the platelet aggregation studies will be discussed as well as the possible relation of this disorder to the Hermansky Pudlack Syndrome seen in oculocutaneous albinism.

Although Storage Pool disease has been well documented in the medical literature in cases of complete albinism this report is, to our knowledge, the first where platelet dysfunction is described associated to selective ophthalmic albinism.

## THE USE OF PROTHROMBIN COMPLEX CONCENTRATE (PROPLEX) IN THE MANAGEMENT OF DENTAL EXTRACTIONS IN PATIENTS WITH FACTOR II COAGULOPATHIES

Jean Fradera, BSMT, Norman Maldonado, MD and José J. Corcino, MD

Prothrombin complex concentrates have been used in the United States since 1969. Although originally developed for the treatment of congenital bleeding disorders of Factors II, VII, IX and X they have become an important tool in the treatment of acquired bleeding diathesis particularly those associated with liver disease. The reported complications associated with the administration of these concentrates are multiple and include thrombosis, anaphylaxis, hepatitis and disseminated intravascular coagulation.

We have documented the successful use of Proplex commercially prepared by Hyland Laboratories, in the management of multiple dental extraction in two patients with severe congenital Factor II deficiency (Hypoprothrombinemia) and in one patient with a non-functional Factor II molecule (dysprothrombinemia).

Congenital hypoprothrombinemia and dysprothrombinemia are rare coagulopathies which require a careful laboratory evaluation to be correctly diagnosed. All patients are severe bleeders and represent a serious problem to the dentist when extractions are required.

The laboratory data relevant to the diagnosis of these coagulation disorders as well as the criteria used in the administration of the Prothrombin Concentrate (Proplex) will be discussed.

## SINDROME DE CUSHING: EXPERIENCIA CLINICA A TRAVES DE 25 AÑOS (1952 - 1977)

Agustín M. de Andino, MD, FACP y Efraín Meléndez, MD. Departamento de Endocrinología y de Medicina, Hospital de la Capital, Centro Médico de Puerto Rico.

Durante los últimos 25 años hemos observado un total de 7 casos del síndrome de Cushing en el Hospital de la Capital y en la práctica privada del autor principal. La serie consiste de 6 mujeres y 1 varón entre 16 y 44 años de edad con una edad media de 31. La sintomatología se extendió desde 3 meses hasta 10 años. Las quejas más prominentes fueron las neuropsiquiátricas variando desde la inestabilidad emocional hasta la psicosis orgánica severa. Otros síntomas de importancia fueron el hirsutismo y la amenorrea en la mujer, la obesidad y el edema variables, y la hipertensión. Hallazgos de laboratorio de importancia fueron los disturbios en el metabolismo de glucosa, la elevación de los 17-hidrocorticoides en la orina, la elevación en el cortisol plasmático con la ausencia del ritmo circadiano y la ausencia de osteoporosis radiográficamente. El plan de estudio diagnóstico ("diagnostic flow sheet") usado en los últimos tres casos a tono con las nuevas técnicas de laboratorio será discutido a plenitud.

Los diagnósticos patológicos en los casos intervenidos fueron hiperplasia adrenal (4), carcinoma adrenal (1), y adrenal normal (1). El caso 7 exhibió un adenoma pituitárico tratado por radioterapia. Se presentarán las nuevas modalidades de tratamiento.

## FAILURE OF GLUCAGON AS TREATMENT FOR ALCOHOL-RELATED PANCREATITIS

Angel Olazábal, MD and Richard Fuller, MD. Veterans Administration Hospital and Cleveland Veterans Adm. Hospital

Previous studies claimed that glucagon an effective treatment for pancreatitis but the studies were either uncontrolled or used histori-



cal controls. To determine if glucagon is efficacious for alcohol-related pancreatitis, we performed a controlled, randomized, double-blind study.

Twenty-six subjects with pancreatitis associated with alcohol ingestion were randomly assigned to receive either glucagon or placebo in addition to intravenous fluids, nasogastric suction, and meperidine as needed. Each subject received either 1.0 mg of glucagon or placebo intravenously as an initial bolus followed by glucagon or placebo in isotonic saline at the rate of 0.25 mg/hr until the patient was pain-free for 24 hours or 120 hours had elapsed since starting treatment. Subject were interviewed and examined at 8:00 a.m., 3:00 p.m., and 11:00 p.m. Blood and urine specimens were obtained for amylase and creatinine determinations at 8:00 a.m., 3:00 p.m., and 11:00 p.m.

There were no statistically significant differences between the group which received glucagon and the group which did not in duration of any of the following: abdominal pain, nausea, anorexia, abdominal tenderness, absence of bowel sounds, fever, renal clearance ratio of amylase to creatinine. We conclude that glucagon in addition to conventional therapy is no better than conventional therapy for the treatment of alcoholic pancreatitis.

#### SEVERE HYPONATREMIA (88 meq/l) WITH FULL RECOVERY

*Herbert I. Goldman, MD. Department of Medicine UPR*

A 76-year old female was found transiently speechless and became bedridden, anorectic and weaker over the 6 weeks prior to admission. During the last week she vomited, was constipated and had not voided in over 24 hours. She was taking chlorthalidone for hypertension. Phys. exam; unable to talk, but cooperative;

dry oral mucosa; fine basal rates; 2/6 systolic murmur. Normal pulse and BP. The electrolytes during the first 6 days were:  $\text{Na}^+$  93, 88, 100, 111, 116, 124, 138 meq/l.  $\text{K}^+$  2.4 rose to 3.1  $\text{Cl}^-$  60 rose to 91.  $\text{CO}_2$  27 stable. With initial treatment for dehydration (500ml of 5 percent dextrose) the  $\text{Na}^+$  fell from 93 to 88 meq/l. Normal saline 4 liters with 80 meq/KCL daily resulted in a progressive rise in  $\text{Na}^+$  to normal. Serum osmolarity was 233 on day 2. Dehydration was suggested by fall in Hct (46 to 34) and in BUN (35 to 9). On day 6 and again on day 14, I.V. fluids were stopped. Each time she became hyponatremic and was restarted on I.V. saline. On day 18 she was able to maintain normal electrolytes off I.V. on a liberal salt diet. During the next 4 years she had no recurrence of this problem. The multiple possible causes for the hyponatremia will be discussed.

#### COMPARACION DE LA ACTIVIDAD EN VITRO POR DISCOS Y DILUCION EN AGAR DE CEFALOTINA (C), CEFAZOLINA (CF), CEFLEXINA (CL), CEFRADINA (CP), CEFACLOX (CC) Y CEFAMANDOLE (CM) EN CONTRA DE 168 ORGANISMOS AISLADOS EN HEMOCULTIVOS

*C. H. Ramírez-Ronda, MD y C. León Valiente, MD. Departamentos de Investigación y Medicina, Hospital de Veteranos y Escuela de Medicina, Universidad de Puerto Rico, San Juan, Puerto Rico.*

La susceptibilidad a las cefalosporinas (CPS) es determinada en muchos laboratorios por el método de difusión de disco usando el disco de 30 ug. Después de encontrar cepas de bacterias resistentes a C por el método de disco que son susceptibles a otras CPS, un estudio prospectivo fue diseñado para comparar la susceptibilidad de 168 organismos aislados en sangre a diferentes CPS. La actividad en vitro de las CPS en contra de cada cepa fue de-

terminada por el método de Kirby-Bauer, usando discos de 30 ug de cada CPS y por el método de dilución en agar. Ambos métodos fueron comparados. Los organismos estudiados incluyeron 60 *Escherichia coli*, 65 *Klebsiella pneumoniae*, 9 *Providencia stuartii*, 6 *Enterobacter spp.* y 28 otros bacilos gram-negativos. Hay una correlación excelente entre la actividad in vitro de cada CPS por los métodos de disco y de dilución en agar. 75 por ciento de las cepas de *E. coli* fueron susceptibles a C, 93 por ciento a CF y 90 por ciento a otras CPS. 49 por ciento de las cepas de *Klebsiella pneumoniae* fueron susceptibles a C, 69 por ciento a CF, 72 por ciento a CC, 90 por ciento a CL y CM y 97 por ciento a CP. Todas las cepas de *Providencia stuartii* y *Enterobacter spp.* fueron resistentes a C, CF, CP y CL. CM inhibió 92 por ciento de estas cepas y CC el 8 por ciento. La CPS más efectiva estudiada fue CM con 91 por ciento de las cepas susceptibles. CM es probablemente la CPS de elección en el tratamiento de infecciones con bacilos gram-negativos cuando el uso de CPS está indicado. A pesar de que el disco de C se usa para probar la susceptibilidad de las CPS, cuando se demuestra resistencia a las CPS en un paciente donde una CPS diferente a C está indicada, se deben hacer estudios de susceptibilidad por métodos de dilución, ya que un número significativo de cepas resistentes a C son susceptibles a otras CPS.

#### STUDY OF LONG-TERM SURVIVAL OF ACUTE LEUKEMIA PATIENTS - REPORT OF 14 CASES

Pedro J. Santiago, MD, Irma Ramírez, MD, Harvey Agosto, MD y Ina Serrán, MD.

The survival of children with acute lymphoblastic leukemia (ALL) has changed dramatically in the past twenty five years. Before

1950 the median time of survival was 3 to 4 months, and about 99 percent of the patients died within twelve months of the diagnosis (1). Since the introduction of effective chemotherapy, a small but significant proportion of children with acute leukemia has survived for five or more years (2, 3) and in the last ten years an increasing number of long-term survivors has been reported by several authors (4-5).

Simone, Aur, Hustu et al reported in 1972 that fifty percent of their patients remained in an initial continuous complete remission for at least 36 months after the diagnosis was made (6). Aur et al published in 1974 data demonstrating that of 132 children with ALL removed from therapy after 2 to 3 years of remission, 84 percent remained free of disease in a mean of 21 months, and range of 1 to 90 months, after cessation of the antineoplastic treatment (7).

How long antineoplastic therapy should be maintained on a child with acute leukemia in continuous complete remission is unknown. There is no convincing evidence that prolonged antineoplastic therapy increases the chances for long-term survival or of possible cure in acute leukemia. On the other hand, some data suggest that unnecessarily prolonged intensive chemotherapy might worsen the prognosis in some patients.

A study conducted by the Children Cancer Study Group A showed that there was no reduction in the relapse rate in patients treated over 2 1/2 years, as compared to controls on whom therapy had been stopped (8). The report by Aur et al mentioned above showed that the relapse rate after 2 1/2 to 3 years of continuous complete remission was unrelated to the use of chemotherapy beyond that point (7).

## WILM'S TUMOR - REVIEW OF 30 CASES

*Harvey Agosto, MD, Pedro J. Santiago, MD, Irma Ramírez, MD, Antonio Frúa, MD, Víctor Marcial, MD and Enrique Marquez, MD*

Of the common childhood cancers, Wilm's tumor has the second highest incidence following leukemia in patients under five years of age. In the United States Wilms tumor occupies the sixth position of all tumors in children below 15 years.

The principal modalities of treatment of Wilm's tumor are surgery, radiation, and chemotherapy, in various combinations. The discovery of actinomycin D has greatly improved the outlook for patients with this malignancy.

Before the discovery of actinomycin D, 25 percent of patients survived the two year risk period. With the use of this antineoplastic agent, 58 to 84.6 percent of the children successfully survive this period, if no metastases are present at operation. But still a long-term survival is low 12.8 percent if metastases are evident at the time of the diagnosis.

Similar improvement in the management of children with Wilms tumor has been observed during the last two decades in Puerto Rico.

Our group in the Pediatric Department of the University Hospital of the University of Puerto Rico School of Medicine has obtained an overall survival rate of 53.3 percent in 30 patients; and 91 percent in 11 patients with stage I disease treated between 1965 and 1975.

The data and experience obtained in the management of these patients is the subject of this paper.

#### CORRELACION ENTRE COLPOSCOPIA, CITOLOGIA E HISTOLOGIA EN LA EVALUACION DE DISPLASIA Y NEOPLASIA CERVICO-VAGINAL

*Mitchel A. Sánchez del Valle, MD, Adrián Colón Larraeunte, MD y Fernando Rampolla Briganty, MD*

Se presenta este estudio prospectivo donde

se analiza material de colposcopia recopilado en alrededor de 450 pacientes femeninas referidas a nuestra Clínica de Anaplasia del Hospital Universitario durante los años 1976-77 para diagnóstico y tratamiento final en nuestra institución. Los pacientes fueron referidos de diversos centros de detección de cáncer por citología anormal o biopsias previas con displasia-neoplasia. Se confirma en este estudio la eficacia y precisión de la colposcopia, junto a la citología, para dirigir biopsia a lugares específicos del cuello uterino y descubrir lesiones tempranas. Se intenta establecer la frecuencia de lesiones colposcópicas relacionadas con los varios grados de displasia y carcinoma in situ. A la vez se enjuicia la confiabilidad de la prueba de Papanicolaou en los casos que resultan positivos por colposcopia e histología para displasia-neoplasia. Se teoriza sobre posibles factores que afecten el diagnóstico citológico.

Se destaca el uso de la colposcopia en el seguimiento de pacientes embarazadas con displasia y carcinoma in situ sin recurrir a la conización. Se discuten las dificultades que encuentra la colposcopia principalmente en la paciente peri o post-menopáusica o en la paciente cuya unión escamo columnar del cuello uterino no es accesible al colposcopio. En estas, la evaluación del canal endocervical es imperiosa antes el diagnóstico citológico.

Se destaca el uso de la colposcopia en el seguimiento de pacientes embarazadas con displasia y carcinoma in situ sin recurrir a la conización. Se discuten las dificultades que encuentra la colposcopia principalmente en la paciente peri o post-menopáusica o en la paciente cuya unión escamo columnar del cuello uterino no es accesible al colposcopio. En estas, la evaluación del canal endocervical es imperiosa antes de recurrir a la conización, pero, no siempre el estudio histológico rinde un diagnóstico satisfactorio. A estos fines se ha diseñado un método en nuestra clínica para recoger y procesar la biopsia de endocuello (ECC) con resultados satisfactorios.



Se describen además las diversas formas de tratamiento para displasia neoplasia en nuestra institución y se alerta ante la marcada tendencia de aparecer estas lesiones en mujeres de temprana edad reproductiva.

### EL VALOR DE LA GAMAGRAFIA OSEA EN LA EVALUACION Y MANEJO CLINICO DE PACIENTES CON CARCINOMA DE LA PROSTATA

*Jeanne Ubiñas, MD, Rafael Román, MD, Aldo Lanaro, MD, José M. Tomé, MD y Víctor A. Marcial, MD*

Esta presentación tiene como objetivo el determinar el valor de la gamagrafía ósea en la evaluación y manejo clínico de pacientes con carcinoma de la próstata. Se analizan los resultados de la gamagrafía ósea en pacientes con o sin síntomas y se relacionan estos con los resultados de laboratorio, los estudios radiográficos y la evolución clínica del paciente.

El estudio estará basado en la experiencia clínica en más de cien pacientes atendidos en el Instituto de Radioterapia del Hospital Metropolitano, el Hospital de Veteranos y el Hospital Universitario. Se presentará una revisión de la literatura médica sobre el mismo tema.

### ACUTE FATTY LIVER OF PREGNANCY, PRESENTATION OF A CASE, AND REVIEW OF LITERATURE

*M. Tellado, MD. Centro Médico de Puerto Rico.*

A twenty-one year old female patient G. II, P. I, Ab. O. developed a fulminant cli-

nical picture of fever and loss of consciousness in her early first trimester of pregnancy. The patient remained lethargic and died on her third hospital day. The laboratory data disclosed altered hepatic functions.

Post mortem studies revealed findings consistent with the so-called acute fatty liver of pregnancy. Comments on the pathogenesis of fatty liver and a review of possible etiologies in this case are discussed.

### FEOCROMOCITOMA MALIGNO CON PRESION ARTERIAL NORMAL E HIPERCALCEMIA

*K. Amézquita, MD y L. Ceballos, MD. Del Centro Médico de Puerto Rico y Escuela de Medicina*

Se presenta un caso de un paciente de 59 años con un cuadro clínico de hipercalcemia que habíase iniciado siete meses antes de su admisión.

Al acentuarse los síntomas, se decide la paratiroidectomía total. En vista de que el cuadro persiste sin grandes modificaciones continúan las exploraciones orientándose hacia un diagnóstico de carcinoma de riñón causando la hipercalcemia. Finalmente, el paciente desarrolla encefalopatía aparentemente secundaria a la hipercalcemia. La posibilidad de metástasis cerebral fue también considerada.

El hallazgo fundamental en el estudio post-mortem es un feocromocitoma maligno de la suprarrenal izquierda.

Se presentará revisión de la literatura destacando la frecuencia y ausencia de elevación de la presión arterial, la posible patogénesis de la hipercalcemia y características ultraestructurales en este tipo de tumor.

## CARCINOMA DE CELULAS GIGANTES DE PULMON. ESTUDIO ULTRAESTRUCTURAL Y REVISION DE LA LITERATURA

K. Amézquita, MD, J. J. Vázquez, MD y L. Ceballos, MD. Centro Médico de P. R., San Juan Veterans Adm. Hospital y Escuela de Medicina.

El carcinoma de células gigantes de pulmón ha constituido una entidad particularmente atractiva por su comportamiento clínico, generalmente fulminante, por su escasa frecuencia y carencia de datos suficientes para precisar su origen epitelial o mesenquimatoso.

Su histogénesis ha sido parcialmente definida a través del estudio ultraestructural y cultivo de tejidos. Sin embargo, aunque su origen ha sido adscrito a células totipotenciales del bronquiolo distal es sorprendente el grado tan elevado de organelas que posee en contraposición a lo que cabría esperar en un tumor de crecimiento tan rápido.

Nuestra paciente, de 51 años de edad, inició su cuadro clínico con una metástasis en región temporo-occipital izquierda.

Se trata de establecer una correlación clínico-patológica y algunos comentarios sobre la biología del tumor.

## CHEMOTHERAPY OF GASTROINTESTINAL CANCER (GI-CA): TEN YEARS EXPERIENCE IN OVER 200 PATIENTS

Antonio J. Grillo-López, MD and Enrique Vélez-García, MD., Instituto de Hematología y Oncología Médica, Hospital Metropolitano, Río Piedras, Puerto Rico and Hematology Section, University Hospital, UPR School of Medicine, Río Piedras, P. R.

Two decades after the introduction of the fluorinated pyrimidines as tumor inhibitory compounds there is yet considerable controversy as to the optimal schedule of administra-

tion of 5-Fluorouracil (5-FU). The conventional schedule (Push) calls for 5 injections on consecutive days followed by half doses on alternate days and yields a 25 percent response rate at the cost of moderate to severe toxicity.

Over the past 10 years we have sequentially studied 4 different schedules and combinations in over 200 patients with advanced GI-CA: I- *Weekly Push* - 12.5 mg/Kg of 5-FU IV push weekly; II- *Drip* - 30 mg/Kg of 5-FU continuous, IV drip daily for 5 days; III- *Drip/Mito* - Drip plus Mitomycin-C (Mito) at 20 mg/M<sup>2</sup> IV; IV- *Drip/Mito/Me CCNU* - Drip/mito plus Methyl CCNU (MeCCNU) at varying dosages. Results are as follows:

Objective Response (or)			
Regimen	Stomach	Pancreas	Colon
I	12/46	2/11	7/37
II	12/21	4/8	7/23
III	0/5	1/3	5/16
IV	2/5	---	3/9

Regimen	Other GI	Overall
I	1/6	22/100
II	4/13	27/65
III	3/6	9/30
IV	0/2	5/16

The best overall response rate (42 percent) was obtained with regimen II (Drip) which has become our standard therapy for advanced GI-CA. A randomized study is being proposed through the Southeastern Cancer Study Group (SEG) to determine whether Drip is superior to Push. Regimen IV needs to be studied further and is the object of an ongoing SEG pilot study.

## THE ROLE OF MAINTENANCE CHEMOTHERAPY AND BCNU (B), CYCLOPHOSPHAMIDE (C), VELBAN (V), PROCARBAZINE (P), AND PREDNISONE (P) IN ADVANCED HODGKIN'S DISEASE (AHD)

*Enrique Vélez García, MD, John R. Durant, MD, Richard Gams, MD, and Ronald Dorfman, MD, for the Southeastern Cancer Study Group, Hematology Section, University of Puerto Rico School of Medicine, University of Alabama in Birmingham, and University of Stanford Medical Center.*

Combination chemotherapy has revolutionized the prognosis in patients with AHD. The majority of patients treated with a combination of nitrogen mustard, Oncovin, procarbazine and prednisone (MOPP) for 6 consecutive months achieve complete remission (CR) regardless of other factors. However, most patients relapse within 18 months after discontinuation of therapy. Reasons for this are not clear but possibilities include: (1) too short a course of therapy, (2) presence of MOPP-resistant foci of occult disease or (3) development of new foci of recurrent disease resistant to known chemotherapeutic agents. Nevertheless, evidence in the literature supporting longer periods of chemotherapy has been conflicting. In order to answer some of these questions, we randomized 324 patients with AHD to (1) no therapy, (2) MOPP for 6 months or to (3) BCVPP for 6 months after an initial 6 month period when all patients were treated with BCVPP as follows: B-100 mg/M<sup>2</sup>, C-600 mg/M<sup>2</sup>, V-5 mg/M<sup>2</sup> IV on day 1 and procarbazine, 100 mg/M<sup>2</sup> po days 1-10, and prednisone, 60 mg/M<sup>2</sup> po days 1-14. 220/324 (68 percent) achieved CR after initial BCVPP. Results with maintenance chemotherapy after CR were superior than with no therapy but one regimen was not better than the other. However, multivariate analysis failed to identify maintenance treatment as an important determinant of either duration of response or survival. Instead, other factors (age > 40, absolute lymphocyte count > 1300 and favorable histologies), not maintenance chemotherapy,

were the major determinants influencing duration of CR. These data compare favorably with other reported series and should be taken into consideration when designing future studies aiming to improve cure rates in AHD.

## END RESULTS IN THE TREATMENT OF ADVANCED GASTROINTESTINAL CANCER WITH 5-FLUOROURACIL DRIP

*Antonio J. Grillo-López, MD, Enrique Vélez-García, MD and Alfred Bartolucci, PhD. Instituto de Hematología y Oncología Médica, Hospital Metropolitano, Río Piedras, P. R. and Dept. of Statistics and Biometry, Emory University, Atlanta, Georgia.*

Since 1973 we have studied and reported on the use of 5-Fluorouracil (5-FU) by continuous systemic infusion (Drip) for 5 days in the treatment of advanced cancer (Bol. Asoc. Med. P. R. 65: 232, 1973). We have been impressed with the apparent superiority of this method of administration as reflected by the overall response rate (OR) of 42 percent that we obtained (ASCO 15: 173, 1974 and 16: 272, 1975). Although large scale, randomized, and well stratified studies have yet to be reported; at least one study has shown superiority of drip (44 percent OR) over the conventional (Push) method of administration (22 percent OR) in colorectal cancer (Cancer 36: 123, 1975). Improved survival, to our knowledge, has not been demonstrated.

We have treated 91 patients with far advanced cancer including 65 with GI-CA utilizing 5-FU drip. Objective responses were seen in 27/65 (42 percent) patients. Survival of responders (from onset of chemotherapy) was significantly superior ( $p = 0.0107$ ) to that of non responders with medians of 8.5 and 5.0 months respectively. There was no statistical difference in survival between sexes, by age group, or by site of primary tumor.

In this study we have shown a statistically significant improvement in survival for respon-



ders to 5-FU drip.

## ADJUVANT COMBINATION CHEMOTHERAPY OF BREAST CANCER IN THE POST-OPERATIVE PERIOD - RESULTS AFTER 3 YEARS FOLLOW-UP

*Enrique Veléz-García, MD and Antonio Grillo-López, MD, Instituto de Hematología y Oncología Médica, Hospital Metropolitano, Río Piedras, P.R.*

Since a majority of patients with breast cancer die with disseminated disease, early chemotherapy as an adjuvant to surgery has been used in many centers recently. In November 1974 we started administering a 5 drug chemotherapy combination consisting of cyclophosphamide (C), methotrexate (M), fluorouracil (F), vincristine (V) and prednisone (P) to patients with clinical stage II breast cancer following mastectomy after evaluation to exclude the presence of metastases. As results of similar trials elsewhere became available, the V and P were eliminated and we continued treatment with CMF in the following schedule: C-400 mg/M<sup>2</sup> IV day 1; M-25 mg/M<sup>2</sup> and F-400 mg/M<sup>2</sup> IV days 1 & 8. Courses are repeated every 28 days on an ambulatory basis for a total of 12 cycles. Patients' psychological acceptance and tolerance has been excellent. So far, 44 patients have entered this study; of these, 32 have completed the planned 12 courses of chemotherapy and are being followed from 3 to 32 months after discontinuation of the chemotherapy regimen. Follow up is performed with monthly physical examinations and x-rays and bone scans every 6 months or as often as necessary to document relapse. Six of the 32 who completed chemotherapy have relapsed, all at distant sites including bones, liver and brain. The 26 patients remaining in remission have been followed for a median of 16 months after discontinuation of therapy. The mean

length of follow up post chemotherapy is 15 months. These data demonstrate that adjuvant chemotherapy may be an effective way of treating micrometastatic disease in breast cancer; however, cautious optimism is necessary until longer periods of follow up have been achieved and until other factors such as hormonal status, receptors, age and role of radiotherapy have been studied. We have recently started a randomized, multi-institutional cooperative group study in an attempt to answer these questions.

## CHEMOTHERAPY OF PROSTATIC AND RENAL CANCER

*Antonio J. Grillo-López, MD, Enrique Veléz García, MD, and Luis Suau, MD, Instituto de Hematología y Oncología Médica, Hospital Metropolitano, Río Piedras, P. R., and University of P. R. School of Medicine, San Juan, P. R.*

Prostatic cancer (CA-PRO) accounts for 12 percent of all cancers in males in P. R. and its incidence has increased steadily in the past 3 decades. Independent of stage at diagnosis, 30 percent of patients will die during the first year. Renal cancer (CA-KID) has a much lower incidence rate but survival is even lower as close to 50 percent of patients die during the first year of their illness.

We have treated 35 patients with CA-PRO and 21 patients with CA-KID with a regimen combining chemotherapy and hormonal therapy as follows: 5-Fluorouracil (5-FU) is given by continuous 5 day IV infusion (drip) at 30 mg/Kg/day and repeated in three weeks. Three weeks after the second course of 5-FU drip maintenance therapy with 5-FU IV weekly is started. Depo Provera is given simultaneously (400 mg IM 3 times/week) for the first 6 weeks.

Objective responses (OR) in CA-PRO are difficult to assess as bone metastases tend to

heal very slowly. However, a 14 percent OR rate was demonstrable. Subjective responses were much more impressive and occurred in 75 percent of patients.

In the patients with CA-KID a 28.5 percent OR rate was obtained including two long lasting complete responses.

Our data shows that chemotherapy has a definite place in the management of the patients with far advanced CA-PRO and CA-KID. Studies are under way to demonstrate whether or not patients in earlier stages will benefit from this type of treatment.

### CARCINOMA DE LA CUERDA VOCAL: EXPERIENCIA CON RADIOTERAPIA

*José M. Tomé, Carmen Zorrilla, MSH, Jeanne Ubiñas, MD, Víctor Marcial, MD y Raúl Marcial Rojas, MD. Instituto de Radioterapia, Hospital Metropolitano.*

Se presenta la experiencia en el Instituto de Radioterapia del Hospital Metropolitano en 60 pacientes con carcinoma de la cuerda vocal. Se analizan los métodos de diagnóstico (clínicos y radiológicos) así como la importancia del patólogo en la clasificación de lesiones precancerosas y carcinomas francos. Todas las lesiones han sido clasificadas en estadios según el sistema T.N.M. Las indicaciones, técnicas y control del tumor por la radioterapia son evaluadas así como el papel de la cirugía como complemento de la radioterapia.

### COMPARISON OF SPLIT-COURSE VERSUS CONTINUOUS IRRADIATION IN CARCINOMA OF THE BASE OF THE TONGUE

*Víctor A. Marcial, MD, José Tomé, MD, Jeanne Ubiñas, MD, Hernando Ortiz, MD, Lawrence Davis, MD, Frank Hendrickson, MD and James Hanley, PhD. Radiotherapy Institute, Metropolitan Hospital.*

This is a report on a prospective collaborative national therapeutic trial in patients

with carcinoma of the base of the tongue. A continuous radiotherapy technique with fractions of 200 to 220 rads per day and total doses of 6000 to 6600 rads, was compared with an interrupted (split) technique consisting of two courses divided by a rest period of 3 weeks. Each course consisted of 10 fractions of 300 rads each.

The patients were submitted to pre-study evaluation according to a written protocol and then they were registered by calling the Group office in Philadelphia. Randomization was made by tumor and node stage, by sex, by institution and by treatment modality.

A total of 142 cases were registered. This report presents the results in terms of tumor control in the tongue and neck, complications and long term survival in each of the two treatment modalities.

### PILOT STUDY OF COMBINED RADIOTHERAPY AND MULTI-DRUG CHEMOTHERAPY IN CARCINOMA OF THE HEAD AND NECK

*Nayda Figueroa, MD, Juan Cintrón, MD, José Corcino, MD, Antonio Grillo, MD, Víctor A. Marcial, MD, E. Vélez García, MD, José M. Tomé, MD, Jeanne Ubiñas, MD, and Luis Vallecillo, MD*

This is the initial analysis of the experience in this pilot study of combined multi-drug chemotherapy and radiotherapy for head and neck cancer. The project has been conducted under the auspices of the Radiation Therapy Oncology Group and the University of Puerto Rico Comprehensive Cancer Center.

It has had the following objectives:

1. To improve the curability of mucosal carcinoma of the head and neck through a combination of three drug chemotherapy followed by radiotherapy; the effectiveness to

be evaluated in terms of tumor control in the head and neck, reduction of the incidence of distant metastases and two year survival.

2. To evaluate toxicity of two courses of three drug chemotherapy (Vincristine, Bleomycin and Methotrexate) preceding radiotherapy.

3. To determine if patients who initially are not technically operable are made operable by this combination of chemotherapy and radiotherapy.

Prior to therapy the patients are evaluated regarding tumor extent, kidney function and general condition. The following patients are excluded: patients with diagnosis of adenocarcinoma, creatine clearance of less than 75 cc/mm., distant metastases, severe cardiac, pulmonary or liver disease, presence of other cancer and previous chemotherapy or radiotherapy.

At the time of this report a total of 28 patients have been registered of which 13 had one chemotherapy course and 15 two courses. The results will be presented in terms of observed toxicity and tumor regression (partial and complete).

## TOXICOLOGIA DEL OJO: QUEMADURAS QUIMICO-VEGETALES MAS FRECUENTES

*Raúl A. Yordán, MD, Escuela de Medicina UPR*

Los ojos están expuestos a múltiples accidentes de naturaleza química, tanto en el hogar como fuera de éste. Las plantas ornamentales más comunmente usadas pueden ser fuente de quemaduras oftálmicas. Este trabajo expone las variedades, modo de acción, composición química de la savia y las lesiones más frecuentes, así como tratamiento y pronóstico.

## MYASTHENIA GRAVIS

*Enrique Piovanetti, MD, Centro Oftalmológico Metropolitano.*

Myasthenia gravis can present itself with ocular signs in 30 percent of cases; which eye changes eventually occur in 75 percent of patients.

Ptosis and diplopia are the symptoms of ocular myasthenia. The ptosis has certain characteristics which help to differentiate it from other causes of lid dropping. The diplopia can result from various oculomotor defects, many of which mimic brain stem disease and can lead the physician into a fruitless search for other diseases.

The intravenous Tensilon test is the diagnostic study of choice, provided precise interpretation is made, and knowing the hazards involved.

Therapy consists of supportive care, anticholinesterases and steroids.

## RETINOPATIA DIABETICA

*José Berrocal, MD*

La retinopatía diabética son los cambios patológicos que ocurren en la retina en pacientes con diabetes.

Clínicamente la retinopatía pasa a través de una serie de etapas que se extienden desde leve retinopatía de trasfondo confinada a la retina misma hasta la invasión de la cavidad vitrea por proliferación de vasos neoformados.

Esta complicación de diabetes está relacionada con la duración de la enfermedad. El control de la glicemia es importante solamente en los cinco primeros años.

Aproximadamente el 1.5 por ciento de la población está afectada con esta enfermedad. Se cree que el 50 por ciento de los pacientes



desarrollan retinopatía diabética.

En los E. U. actualmente hay 200,000 personas ciegas por esta condición. Para el año 2,000 se anticipa que más de medio millón de personas estarán ciegas debido a un aumento anual de 9 por ciento en la población diabética.

El tratamiento que ha probado ser efectivo en prevenir la ceguera es la fotocoagulación de la retina.

Esta fotocoagulación se lleva a cabo preferiblemente con el rayo laser de argon. La Escuela de Medicina de la Universidad de Puerto Rico participó en el estudio de investigación clínica que a nivel nacional se llevó a cabo y en el cual se probó su efectividad.

## LA PUPILA BLANCA EN LA INFANCIA

*Charles J. Lee, Sr.*

El retinoblastoma es el tumor maligno más frecuente del ojo en la edad pediátrica. El signo más frecuente es el reflejo blanco pupilar. Aunque el retinoblastoma es un tumor agresivo, el diagnóstico temprano se acompaña de una curabilidad muy alta. Hay otras condiciones en la infancia que también se acompaña de leucocoria. Granulomas producidos por *toxocara canis*, la fibroplasma retrolenticular, las cataratas congénitas, la enfermedad de Coat, la hiperplasia persistente del vitreo primaria y otras malformaciones congénitas son algunas de las condiciones que se pueden confundir con el retinoblastoma. Es importante que el pediatra, y el generalista refieran rápidamente cualquier caso sospechoso de retinoblastoma.

## SUBMASSIVE LIVER NECROSIS PROBABLY DUE SECOND EXPOSURE TO HALOTHANE

*M. Tellado, MD, Hospital Universitario Río Piedras, P.R.*

A forty-two year old female underwent two operations for peptic ulcer disease. The first operation was done two years ago, for perforated duodenal ulcer. The second operation was 2 years later (1977) for gastric outlet obstruction. She received halothane as anesthetic agent during both procedures. Following the second operation and after five days of an uneventful post-operative course the patient suddenly developed severe liver function abnormalities and lapsed into hepatic coma. She remained in this state throughout and died 14 days after surgery.

The pathologic findings consisted of submassive liver necrosis. Several studies done to identify an infectious etiology were found to be negative. The principal causal agent, thus, appears to be a toxic one although, the frequency of halothane intoxication is rare (1.4 percent). This case points, as, the immediate cause of the demise, a reexposure to halothane.

## THE PSYCHO-PROPHYLACTIC METHOD.

*Luis A. Bernal-Castroverde, MD*

We are aware of several psychosomatic treatments for the elimination of pain at childbirth: Schultz, Hypnosis, etc., and also certain types of exercises that contribute to the physical improvement of the pregnant woman, but not to the prophylaxis of childbirth.

The Psychoprophylactic treatment is essentially EDUCATIVE, and language is its fundamental basis.

It is the author's opinion that such psychosomatic procedures are confined within the small obstetric field, purely for the suppression of delivery pain, not for its prophylaxis.

These methods are of positive value, but the Psychoprophylactic Treatment has a much wider field, being located in the field of Mental Health. We consider it as a Psycho-vaccine, a

new field in medicine: Psycho-Obstetrics.

In our long practice we have found a frustrating condition in both husband and wife.

The education of our society through centuries has been a Negative Reflex Conditioning with the use of the second signal system (Pavlovian terminology). Only using this same scientific system it is possible to change the attitude of the couples and, in a longer scale, that of our society. The first objective is IMMEDIATE, the second is MEDIATE.

### FROZEN SEMEN INSEMINATION

Walter M. Pinedo, MD, FACOG, Rafael Rodríguez Acevedo, MD. Mayaguez Medical Center, Mayaguez, P. R.

Donor insemination with frozen semen results in about 50 percent success rate. The ready availability of semen and the use of the same donor on repeated occasions for a particular woman are major advantages. Disadvantages includes ultrastructural changes in the acrosome areas of spermatozoa and a 50 percent reduction in the original mortality of spermatozoa frozen and subsequently thawed.

The only true indication for artificial insemination is the psychologically and physiologically normal female, married to a psychologically healthy male who for whatever reason has total azoospermia (Behrman). To this should be added men with necrospemria, men with severe oligospermia with infertility of long duration, men with circulation sperm antibodies, and men with previous vasectomy.

The interview with the patient and her husband is of utmost importance. They must request the procedure, understand the procedure, accept the responsibility for any abnormal or defective child, and accept the offspring as their own. Legal, moral and religious aspects of A.I.D. will be discussed.

### LA CALIDAD DE LA VIDA Y LA SALUD MENTAL EN PUERTO RICO: UN ESTUDIO EPIDEMIOLOGICO DE PLANIFICACION Y EVALUACION

Michael A. Woodbury, Sociedad de Siquiatría de Puerto Rico

El trabajo describe el Modelo Epidemiológico utilizado para conseguir datos estadísticos sobre los cuatro ambientes ecológicos (físico externo, físico interno, psicológico y societal), utilizando los 76 municipios de Puerto Rico como unidades geográficas, administrativas y estadísticas. El informe describe, compara y correlaciona tres estudios hechos en Puerto Rico por la Comisión:

1. Un Sistema de 50 indicadores describiendo objetivamente la calidad de la vida en los municipios de Puerto Rico.

2. Estudio de la Felicidad en Puerto Rico, utilizando la Muestra Básica del Departamento de Salud de Puerto Rico.

3. Resultados de un cuestionario enviado a los Alcaldes de los Municipios de Puerto Rico para conseguir una evaluación de los problemas con que éstos se confrontan y de los servicios que se proveen para resolverlos.

En conclusión, se describe un sistema estadístico de planificación y evaluación de programas de salud y salud mental para Puerto Rico.

### HOT AUTONOMOUS THYROID NODULE WITH COMPLETE HEMIAGENESIS OF THE REMAINING LOBE

Gabriel R. Martínez Rovira, MD. Doctor's Medical Center, Santurce, P. R.

The median thyroid anlage from which most of the gland develops, and the two lateral thyroid parts may give rise to certain particular anomalies which fall into two categories:

1. Failure of the gland or part of it to develop.

2.. Differentiation in abnormal location.

We have recently investigated an 11 year old male who presented a mass in the area of the right lobe of the thyroid gland. Pertinent

studies revealed this lesion to be a solitary autonomous non toxic nodule associated with complete hemiagenesis of left thyroid lobe.

The embryologic and anatomic features together with clinical implications will be the subject of the discussion in this unusual case.



## FROM THE AMERICAN COLLEGE OF PHYSICIANS INTERNISTS MEET IN PUERTO RICO IN OCTOBER

Philadelphia, Pa. — Specialists in internal medicine and related medical fields from Puerto Rico will take part in a two-day scientific meeting in Ponce on October 14-15.

The Puerto Rico Regional Meeting of the American College of Physicians (ACP) is designed to bring physicians up-to-date on late developments in the field of internal medicine. It is one of 40 such sessions held each year throughout the United States and Canada by the 37,000-member medical specialty society.

One of the prime purposes of the American College of Physicians, which is headquartered in Philadelphia, Pa., is the continuing education of practicing physicians. In addition to regional meetings, it sponsors a four-day national meeting, postgraduate courses and publishes the monthly *Annals of Internal Medicine*.

Physicians who attend the regional meeting are eligible for credit toward the American Medical Association Physician's Recognition Award in Category No. 1.

In charge of planning for the ACP's Puerto Rico Regional Meeting is José M. Torres-Gómez, MD, FACP, San Juan, who serves as the medical specialty society's representative in Puerto Rico.

---

## FROM AHA NEWS:

### LAETRILE OVERDOSE CAUSES CYANIDE POISONING

Chicago — Those who insist on using laetrile as a treatment for cancer are advised to keep the tablets in childproof containers and to have a cyanide resusci-

tation kit quickly available.

Laetrile, or amygdalin, is an extract of apricot pits used to treat cancer. Most medical authorities have declared it valueless. And now it is also known to be dangerous.

Death of an 11-year old girl from accidentally swallowing laetrile tablets is reported in the Aug. 8 Journal of the American Medical Association.

A trio of Buffalo, N. Y. physicians report that the child swallowed from one to five tablets of the product. It belonged to her father, who has cancer. The tablets were thought to be harmless by the parents and were contained in a vial along with an assortment of vitamin tablets, the doctors say.

The child became listless within half an hour after swallowing the tablets, and vomited. When breathing became difficult and the child began to lose consciousness, the mother rushed her to a hospital, extensive and heroic treatment measures were instituted, but the child died after 72 hours.

Death was from cyanide poisoning. Laetrile is made from the pits of apricots, which contain cyanide.

---

## RISKS OF BREAST CANCER WEIGHED FOR PATIENTS

Chicago — What are my chances of getting breast cancer?

This is the question that most women ask their doctor sometime during their lives.

In the July 25 Journal of the American Medical Association, Theodore C. Bernstein, MD, cancer specialist of the Scripps Clinic and Research Foundation, La Jolla, Calif., offers some guidelines to physicians to help them answer the question.

In one of every 15 women, breast cancer will develop, Dr. Bernstein says. Women with an early

# THREE-IN-ONE THERAPY AGAINST TOPICAL INFECTION

## Neosporin<sup>®</sup> Ointment

(Polymyxin B-Bacitracin-Neomycin)

This potent broad-spectrum antibacterial provides overlapping action to help combat infection caused by common susceptible pathogens (including staph and strep). The petrolatum base is gently occlusive, protective and enhances spreading.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

### Neomycin

*Staphylococcus*  
*Haemophilus*  
*Klebsiella*  
*Aerobacter*  
*Escherichia*  
*Proteus*  
*Corynebacterium*  
*Streptococcus*  
*Pneumococcus*

### Bacitracin

*Staphylococcus*  
*Corynebacterium*  
*Streptococcus*  
*Pneumococcus*

### Polymyxin B

*Pseudomonas*  
*Haemophilus*  
*Klebsiella*  
*Aerobacter*  
*Escherichia*

*In vitro* overlapping antibacterial action of  
Neosporin<sup>®</sup> Ointment (polymyxin B-bacitracin-neomycin).

## Neosporin<sup>®</sup> Ointment

(Polymyxin B-Bacitracin-Neomycin)

Each gram contains: Aerosporin<sup>®</sup> brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs; in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is

affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.





2010



# When choosing a diuretic for day-in-day-out hypertension control with comfortable compliance...

The agent you choose in mild to moderate essential hypertension should offer (1) long-term effectiveness, (2) patient comfort, and (3) compliance.

## Zaroxolyn offers all three.

**Effectiveness:** In several long-term studies<sup>1,2,3</sup> Zaroxolyn brought moderately elevated blood pressure (average 167/113 mm Hg) down to the range of normotension—and held it there for up to four years.

**Comfort-in-use:** One investigator noted, "Patient cooperation was surprisingly good for a study of such duration. The once-daily schedule with metolazone (Zaroxolyn) no doubt contributed to patient compliance."

**Overall compliance** with Zaroxolyn is good—very good. An analysis of controlled clinical studies involving 188 Zaroxolyn patients showed that only eight discontinued therapy because of side effects. That's a discontinuation rate of only 4.3%, and broader clinical experience appears to substantiate this low rate.<sup>3</sup>

## Long-acting **Zaroxolyn**<sup>®</sup> (metolazone) Pennwalt 2½ mg, 5 mg and 10 mg tablets once-daily antihypertensive diuretic

Recommended initial dosage in mild to moderate essential hypertension—2½ to 5 mg once daily

Before prescribing, see complete prescribing information in the package insert, or in PDR, or available from your Pennwalt representative. The following is a brief summary. **Indications:** Zaroxolyn (metolazone) is an antihypertensive diuretic indicated for the management of mild to moderate essential hypertension as sole therapeutic agent and in the more severe forms of hypertension in conjunction with other antihypertensive agents. Also, edema associated with heart failure and renal disease. **Contraindications:** Anuria, hepatic coma or precoma, allergy or hypersensitivity to Zaroxolyn. Or, as a routine in otherwise healthy pregnant women. **Warnings:** In theory cross-allergy may occur in patients allergic to sulfonamide-derived drugs, thiazides or quinethazone. Hypokalemia may occur, and is a particular hazard in digitalized patients; anginous or fatal arrhythmias may occur. Hyponatremia and hyperuricemia may be noted or precipitated. Considerable potentiation may occur when given concurrently with furosemide. When used concurrently with other antihypertensives, the dosage of the other agents should be reduced. Use with potassium-sparing diuretics may cause potassium retention and hyperkalemia. Administration to women of childbearing age requires that potential benefits be weighed

against possible hazards to the fetus. Zaroxolyn appears in the breast milk. Not for pediatric use. **Precautions:** Perform periodic examination of serum electrolytes, BUN, uric acid, and glucose. Observe patients for signs of fluid or electrolyte imbalance. These determinations are particularly important when there is excessive vomiting or diarrhea, or when parenteral fluids are administered. Patients treated with diuretics or corticosteroids are susceptible to potassium depletion. Caution should be observed when administering to patients with gout or hyperuricemia or those with severely impaired renal function. Hyperglycemia and glycosuria may occur in latent diabetes. Chloride deficit and hypochloremic alkalosis may occur. Orthostatic hypotension may occur. Dilutional hyponatremia may occur in edematous patients in hot weather. **Adverse Reactions:** Constipation, nausea, vomiting, anorexia, diarrhea, bloating, epigastric distress, intrahepatic cholestatic jaundice, hepatitis, syncope, dizziness, drowsiness, vertigo, headache, orthostatic hypotension, excessive volume depletion, hemoconcentration, venous thrombosis, palpitation, chest pain, leukopenia, urticaria, other skin rashes, dryness of mouth, hypokalemia, hyponatremia, hypochloremia, hypochloremic alkalosis, hyperuricemia, hyper-

glycemia, glycosuria, raised BUN or creatinine, fatigue, muscle cramps or spasm, weakness, restlessness, chills, and acute gouty attacks. **Usual Initial Once-Daily Dosages:** mild to moderate essential hypertension—2½ to 5 mg; edema of cardiac failure—5 to 10 mg; edema of renal disease—5 to 20 mg. Dosage adjustment may be necessary during the course of therapy. **How Supplied:** Tablets, 2½, 5 and 10 mg

### References:

1. Dornfeld L, Kane R: Metolazone in essential hypertension. The long-term clinical efficacy of a new diuretic. *Curr Ther Res* 18 527-533, 1975
2. Cangiano JL: Effects of prolonged administration of metolazone in the treatment of essential hypertension. *Curr Ther Res* 20 745-750, 1976
3. Data on file: Medical Department, Pennwalt Prescription Products

**PENNWALT**  
Pennwalt Prescription Products  
Pharmaceutical Division  
Pennwalt Corporation  
Rochester, New York 14603



# COLBY PROCLAIMS WOMAN SUFFRAGE

Signs Certificate of Ratification  
at His Home Without  
Women Witnesses.

MILITANTS VEXED AT PRIVACY.

Wanted Movies of Ceremony,  
But Both Factions Are

WASHINGTON, Aug. 26, 1920—  
The struggle for Women



## TRUMAN CLOSES UNITED NATIONS CONFERENCE WITH PLEA TO TRANSLATE CHARTER INTO DEEDS

### NEW WORLD HOPE

President Hails 'Great  
Instrument of Peace,'  
Insists It Be Used

### HISTORIC LANDMARK

Meeting Gives Standing  
Ovation as Executive  
Pictures Peace Gain

"If we fail to use it," he declared  
to the solemn final meeting of the  
delegates, 'we shall betray all of  
those who have died in order that  
we might meet here in freedom and  
safety to create it.'

"If we seek to use it selfishly—for  
the advantage of any one nation or  
any small group of nations—we  
shall be equally guilty of that be-  
trayal."

#### Fervent Interpolation

The President, speaking in the  
auditorium of the War Memorial  
Opera House, built in memory of  
sons of the Golden Gate city who  
gave their lives in the first World  
War, in which he himself served,  
seemed to give unconscious expres-  
sion to the solemn feeling of the  
occasion when, at the outset of his  
speech, he interpolated the words,  
half a hope, half a prayer:

"Oh, what a great day this can

# Social Security Bill Is Signed Gives Pensions to Aged, Jobless

Roosevelt Approves Message Intended to Benefit 30,  
Persons When States Adopt Cooperating Laws—He  
the Measure 'Cornerstone' of His Economic Program

## SENATE APPROVES 18-YEAR OLD VOTE IN ALL ELECTIONS

Amendment to Constitution  
is Sent to House, Where  
Passage is Expected

WASHINGTON, March 10,  
1971—The Senate approved  
today, 94 to 0, and sent to

WASHINGTON, Aug.  
The Social Security Bill,  
a broad program of un-  
insurance and old age  
and counted upon to be  
20,000,000 persons, beca  
day when it was signed  
dent Roosevelt in the p  
those chiefly responsibl  
ting it through Congress

Mr. Roosevelt called th  
"the cornerstone of a  
which is being built to  
means complete

## the Draft Ends No

WASHINGTON, Jan. 27,  
1973—"With the signing of  
the peace agreement in  
Paris today, and after re-

# PATIENT PACKAGE INSERTS: A CONCEPT WHOSE TIME HAS COME?

*The consumer's right to know is an irreversible and desirable trend of the Seventies. It extends, and properly, to a patient's right to know more about his or her prescription medications. One way, gaining favor, is through patient package inserts. Wisely-prepared and properly distributed when medically indicated, they could markedly improve patient knowledge and drug therapy—laudable goals by anyone's standards.*

*The PMA endorses these goals and will work with government, the health professions and consumers to achieve them.*

## **The Advantages**

The concept holds promise of benefits: better patient understanding of the product prescribed, better adherence to the treatment plan, and more awareness of possible side reactions.

Every doctor has had patients who fail to finish antibiotic regimens because they feel better. Some patients assume that if one tranquilizer or analgesic is good, two may be twice as good. Still others fail to report dizziness while on antihypertensive therapy—and so on.

Problems like these might arise less often if the patient received written information in addition to verbal instructions. Some studies suggest that patients are more receptive to such materials, and they more often understand the verbal instructions and follow them, when inserts are used.

## **The Disadvantages**

There are also some potential problems. Obviously, the inserts must be clearly phrased, without extraneous or complex detail. How much information

is enough? How can it be kept current? Should all patients receive the same information? Should inserts be included with all drugs? Should only potential problems be listed or are patients better off with a "fair balance" presentation that describes usefulness as well as drawbacks?

These and similar questions require answers, since model inserts have yet to be properly developed and tested. Despite the need for these studies, the FDA is proceeding prematurely with inserts on selected products. We think the Congress is the only place where the matter can be given the proper legal status and direction, particularly since it represents a conceptual change in the legal, medical and social framework of the nation's prescription drug information system.

## **The Solution**

The PMA believes that carefully-devised pilot studies of various kinds of inserts are needed. They should be developed and implemented with full participation by doctors, pharmacists, consumers, communications experts and the drug industry. Such studies will provide reliable pathways to follow, so that inserts will be useful aids to medical practice.

And particularly we think that you should be closely involved in this debate and in these studies and decisions. Otherwise, people with less experience and qualifications may control the purposes, content and use of a tool with considerable promise for improved patient care. It could make a difference in your practice tomorrow, and more importantly, in the health of your patients.

**PMA**

THE PHARMACEUTICAL MANUFACTURERS ASSOCIATION  
1155 FIFTEENTH ST., N. W., WASHINGTON, D. C. 20005



menarche and those with menopause at 50 years and older have about 1 1/2 times greater risk than those having natural menopause under the age of 45 years. Removal of the ovaries in a woman aged 40 years or less decreases the risk about 50 percent.

Risk is tripled when first pregnancy occurs after the mother is 35 years of age, he says. Women who have never married are at increased risk. Women who are fat have increased risk.

Birth control pills and hormones given after menopause have been implicated in cancer, but the relationship is not established, Dr. Bernstein says. However, there is enough of an association to suggest that estrogens should not be used by high risk patients.

Prior cancer of the uterus, ovary or colon increases risk of breast cancer. The most common premalignant lesion is cancer of the opposite breast. One in ten of those having cancer in one breast will develop cancer in the other.

Risk of breast cancer varies geographically. In Japan women have a much lower rate than in America. When Japanese women migrate to America, the incidence increases after several generations. Exposure to irradiation by mammograph "probably increases the risk, especially in premenopausal women."

Heredity plays a major role in breast cancer risk. Children of women having bilateral breast cancer may have a 50 percent chance of having the disease. Period of highest risk in women is between the ages of 20 and 40 years. But in women with no heredity risk, the probability of breast cancer development rises with advancing age.

---

#### ALCOHOLISM MORE DANGEROUS TO WOMEN THAN MEN

Chicago — Alcoholism is more damaging to women than to men, says a report in the July issue of Archives of Internal Medicine, a scientific publication of the American Medical Association.

Scientists at the University of Toronto, Canada, report on a study of physical disease profiles of 135 female and 737 male alcoholics. The patients were similar in age, social class and referral pattern.

Although the women had been drinking hazarously for fewer years, the prevalence of most diseases was similar in men and women, says Mary Jane Ashley, MD, and colleagues.

There was an excess of anemia in women, and an excess of fatty liver and chronic obstructive lung disease in men. Women had double the frequency of cirrhosis of the liver.

The average duration of hazardous drinking before the first occurrence of almost all illness events was shorter in women, 14.1 years to 20.2 years.

"These findings suggest that the development of physical morhidity in relation to hazardous drinking may be accelerated in women," Dr. Ashley concludes.

There are indications that the incidence of alcoholism in women is increasing. The suggestion that the development of physical morhidity may be accelerated in female compared to male alcoholics should be a cause for concern and a stimulus for the further clarification of sex differences in the physical disease consequences of alcoholism, she says.

---

#### DRUG SMUGGLERS DIE AS SWALLOWED BAGS OF COCAINE BURST IN STOMACH

Chicago — Two young men died and another became seriously ill when their efforts to smuggle cocaine into the United States by swallowing small rubber containers went awry, says a report in the Sept. 26 Journal of the American Medical Association.

A current method to conceal the drug during customs clearance is to place the white powdery substance in condoms that are then swallowed. The packets are subsequently recovered from stools.

The problem comes when one of the packets breaks inside the smuggler, releasing a large overdose of the drug into his body.

The three cases occurred in Miami, Fla., and are reported by physicians from University of Miami-Jackson Memorial Hospital Medical Center.

Two of the men, one 17 and the other 22, were found dead in Miami hotel rooms shortly after arriving by plane from Colombia in South America. At post-

mortem, the 17-year-old was found to have swallowed 53 condoms filled with cocaine. One of them had broken. An autopsy on the 22-year old found 75 packets of cocaine in various areas of the gastrointestinal tract. Eight had ruptured.

A 31-year-old man was brought to Jackson Memorial Hospital after his arrest at Miami International Airport by narcotics agents for attempted smuggling of cocaine. He had admitted swallowing six condoms filled with cocaine. X-ray showed foreign bodies in his stomach. An effort to remove one of the sacks by endoscope, a tube inserted into the stomach, failed when the packet broke. The patient became seriously ill from the cocaine overdose. Surgeons operated to remove the bags from his stomach and he eventually recovered.

Carlos A. Suárez, MD, and colleagues point out that cocaine has been used by the Indians of Peru and Bolivia for at least 1,200 years. It is extracted from the leaves of the coca plant and is used by the Indians as a stimulant.

Cocaine is highly toxic and physicians must use drastic means to remove it from the stomach if swallowed, Dr. Suárez says. Surgery likely is the most effective method.

---

#### RED BLOOD CELLS PREFERRED TO WHOLE BLOOD IN TRANSFUSIONS

Chicago — Indiscriminate use of whole blood transfusions is discouraged in the newly revised edition of *General Principles of Blood Transfusion*, the Amer-

ican Medical Association's manual on blood for the practicing physician.

The risk to the patient from transfusion is reduced considerably when only the red blood cells rather than whole blood is administered, the AMA manual points out. Use of only the red cells reduces the incidence of circulatory overload, the most common cause of transfusion injury.

Kenneth W. Sell, MD, chairman of the former AMA Committee on Transfusion and Transplantation, points out that blood banks now provide the various components of blood that have already been separated in the laboratory — red cells, platelets, white cells and plasma. The physician may select only those components that the patient needs, and thus avoid giving whole blood much of the time.

First published in 1963, the manual has undergone several revisions as blood practices changed, the 1977 edition being the fourth edition.

Every blood transfusion carries an element of risk of hepatitis and other diseases in addition to the danger of incompatibility that can be disastrous for an individual patient.

"As with a drug with known side effects, the physician must weigh the potential danger against the expected benefit before ordering a transfusion. A blood transfusion should never be ordered or given unless it is worth the risk."

Editor of the new edition is Tibor J. Greenwalt, MD, medical director of the blood program of the American Red Cross, of Washington, D. C.

Copies of the book (request publication OP 267) may be ordered from the American Medical Association, 535 N. Dearborn St., Chicago, Ill. 60610. Price of individual copies is \$3.00.

LISTA DE ANUNCIANTES

BURROUGHS WELLCOME  
Neosporin, Septra

CIBA PHARM.  
Vioform - HC

PENNWALT CORP.  
Zaroxolyn

PHARM. MFG. ASSOC.  
Institunional

ROCHE LAB.  
Librium, Valium

ROERIG & CO.  
Antivert

RORER INTERNATIONAL  
Maalox Plus

SMITH, KLINE & FRENCH  
Dyazide

NOS VIERON...  
EN LA  
TELEVISION

**VACACIONES  
DIFERENTES  
PARA TODA  
LA FAMILIA  
en la...**

**NIEVE**



**2  
TOURS  
ESPECIALES  
AL...**

**"SKIING"  
"ICE-SKATING"  
"TOBOGGANING"  
"SNOWMOBILES"  
"HORSE-DRAWN  
SLEDS"  
"CROSS  
COUNTRY  
SKIING"**

**King's  
Grant  
Inn**

**A PRECIOS RAZONABLES  
QUE INCLUYEN TODO!**

PARA MAS INFORMACION

**EDDIE ORTIZ** % CONTACTO  
CALLE HOARE 602, TEL.  
SANTURCE, P.R. 00908 722-2196  
EXT. #1



# In recurrent urinary tract infections due to susceptible organisms\*

## Septra<sup>®</sup> DS Tablets

Each tablet contains:

**160 mg trimethoprim and  
800 mg sulfamethoxazole**

## Septra<sup>®</sup> Suspension

Each teaspoonful (5 ml) contains

**40 mg trimethoprim and  
200 mg sulfamethoxazole**

### In vitro antibacterial action well balanced by clinical success

- convenient b.i.d. dosage schedule helps insure patient compliance
- pleasantly flavored cherry suspension available for children
- Septra and Septra DS now available in new *small-size* tablets

### Rx guidelines

- during therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination
- contraindicated in children under two months old
- see prescribing information for complete guidelines

\*It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

## Septra<sup>®</sup>

Tablets and Suspension

**Indications and Usage: Urinary Tract Infections:** Urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

**NOTE:** The increasing frequency of resistant organisms limits the usefulness of antibacterials, especially in these urinary tract infections.

The recommended quantitative disc susceptibility method (*Federal Register* 37: 20527-29, 1972) may be used to estimate bacterial susceptibility to Septra. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Septra therapy. "Intermediate susceptibility" also indicates that response is likely and "Resistant" that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

**Precautions:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarthritis nodosa and L. E. phenomenon have occurred. Due to certain chemical similarities to some

goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

**Dosage and Administration:** Not recommended for use in infants less than two months of age.

**Adults:** The usual adult dosage for the treatment of urinary tract infections is one double strength tablet or two regular tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. Shake suspension well before using.

**Children:** Recommended dose is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses for 10 days. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older

Weight		Dose — every 12 hours	
lb	kg	Teaspoonfuls	Tablets
20	9	1 (5 ml)	1/2
40	18	2 (10 ml)	1
60	27	3 (15 ml)	1 1/2
80	36	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the Usual Dosage Regimen
Below 15	Use Not Recommended

**Supplied:** Septra DS (Double Strength) tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole — bottles of 60 tablets and unit dose packs of 100. Septra tablets containing 80 mg trimethoprim and 400 mg sulfamethoxazole — bottles of 40, 100, 500, and 1000 tablets and strip packages of 100 individually packed tablets. Oral suspension, containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored — bottles of 450 ml.

**References:** 1. PMR Bacteriologic Report — urine cultures only. National summary Dec 1975, Jan 1976, Feb 1976. (From 200 acute care hospitals of 100 beds or more.) Data on file, Burroughs Wellcome Co.  
2. Data on file, Burroughs Wellcome Co.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

# The Septra<sup>®</sup> Ba

Each tablet contains:

80 mg trimethoprim and 400 mg sulfamethoxazol

## A strong in vitro record<sup>1</sup>

### E coli

**Septra 95%**

of 220517 isolates

**Cephalosporin 79%**

of 358025 isolates

**Ampicillin 74%**

of 351311 isolates

**Nitrofurantoin 95%**

of 338756 isolates

### Proteus sp

**Septra 91%**

of 66163 isolates

**Cephalosporin 81%\***

of 106281 isolates

**Ampicillin 77%\***

of 104437 isolates

**Nitrofurantoin 13%**

of 100829 isolates

\*Indicated in approved drug information  
for *Proteus mirabilis* only.

### Enterobacter

**Septra 87%**

of 9896 isolates

**Cephalosporin 32%†**

of 14986 isolates

**Ampicillin 15%†**

of 14036 isolates

**Nitrofurantoin 66%**

of 14219 isolates

†Not indicated in approved drug information.

### Klebsiella

### pneumoniae

**Septra 87%**

of 46279 isolates

**Cephalosporin 85%**

of 76898 isolates

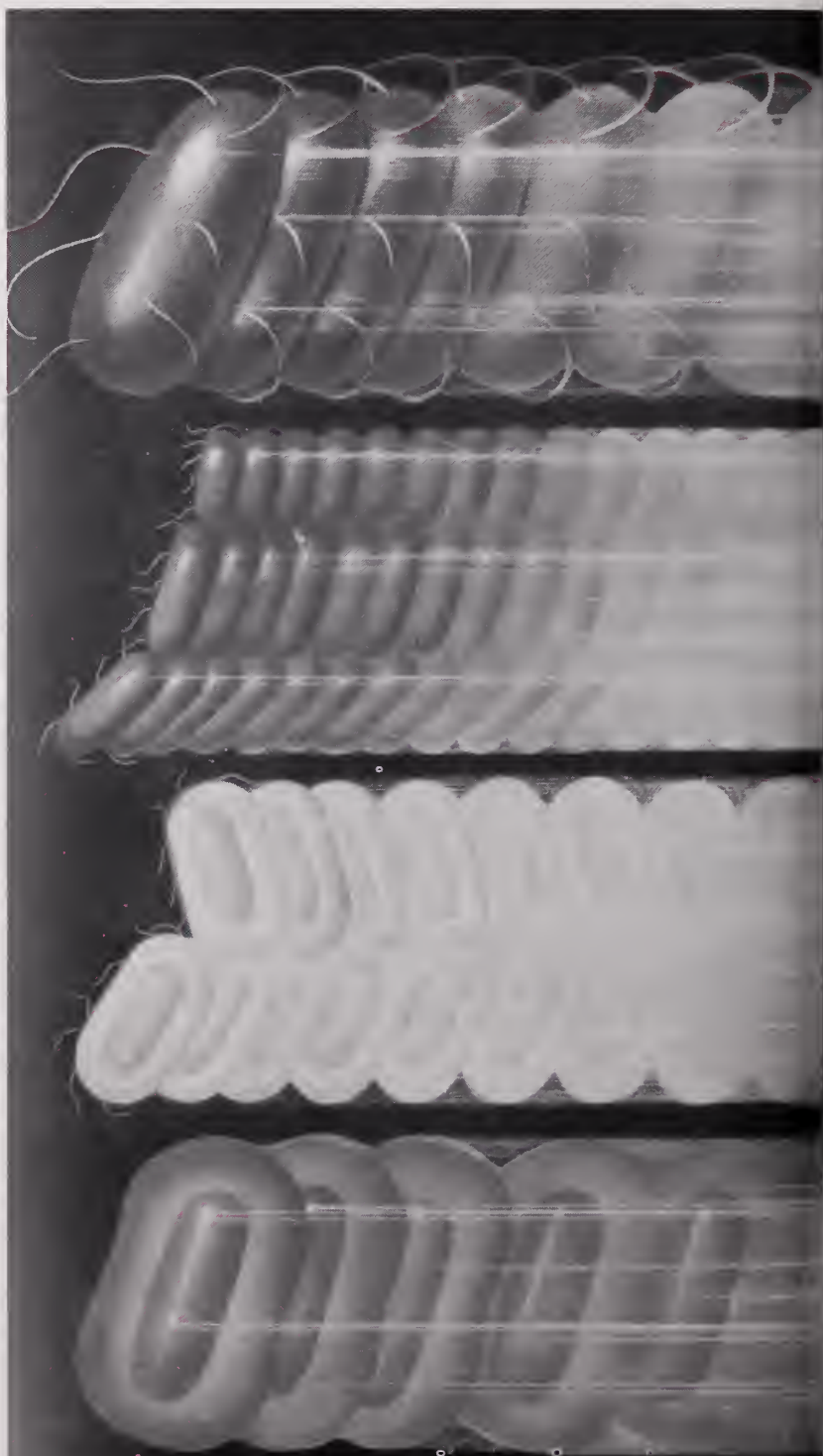
**Ampicillin 5%†**

of 76026 isolates

**Nitrofurantoin 68%**

of 72030 isolates

†Not indicated in approved drug information.



**In vitro activity does not necessarily  
imply a correlation with in vivo results.**



# ance of Power

## A consistent in vivo response

### **Septra outperformed cephalixin**

In a study of 148 patients with recurrent urinary tract infections,<sup>2</sup> bacteriologic response rate on day 14 of therapy<sup>††</sup> was 99% with Septra, compared to 94% with cephalixin.<sup>5</sup> This superiority of response to Septra occurred in spite of a built-in "handicap": Infecting organisms had to be susceptible *in vitro* to cephalixin, but not necessarily to Septra. Drug regimens consisted of either two Septra tablets b.i.d. or one 250 mg cephalixin pulvule q.i.d.

<sup>††</sup>Results derived from urine cultures done at the midpoint of a 28-day study, since recommended duration of Septra therapy is 14 days.

<sup>5</sup>Criterion for infection: 100,000 or more organisms/ml urine, criterion for clear culture: 1000 or fewer organisms/ml urine.

### **Septra outperformed ampicillin**

In a study of 10-day therapy in 156 patients with recurrent urinary tract infections,<sup>2</sup> clear culture was maintained four days after therapy ended in 81% of patients treated with Septra, compared to 76% of those treated with ampicillin.<sup>5</sup> These results gain added significance considering that causative organisms not susceptible *in vitro* to ampicillin were excluded, but no such advantage was afforded Septra. Drug regimens consisted of either two Septra tablets b.i.d. or one 500 mg ampicillin capsule q.i.d.

<sup>5</sup>Criterion for infection: 100,000 or more organisms/ml urine, criterion for clear culture: 1000 or fewer organisms/ml urine.

### **Septra outperformed nitrofurantoin (macrocrystals)**

In a study of 289 patients treated for 14 days for recurrent urinary tract infections,<sup>2</sup> bacteriologic response (measured eight days after therapy ended) to Septra was 94%, compared to 90% with nitrofurantoin.<sup>5</sup> Drug regimens consisted of either two Septra tablets b.i.d. or one 100 mg capsule of nitrofurantoin macrocrystals q.i.d.

<sup>5</sup>Criterion for infection: 100,000 or more organisms/ml urine; criterion for clear culture: 1000 or fewer organisms/ml urine.

### **In vitro antibacterial action well balanced by clinical success**

# **Septra<sup>®</sup> DS**

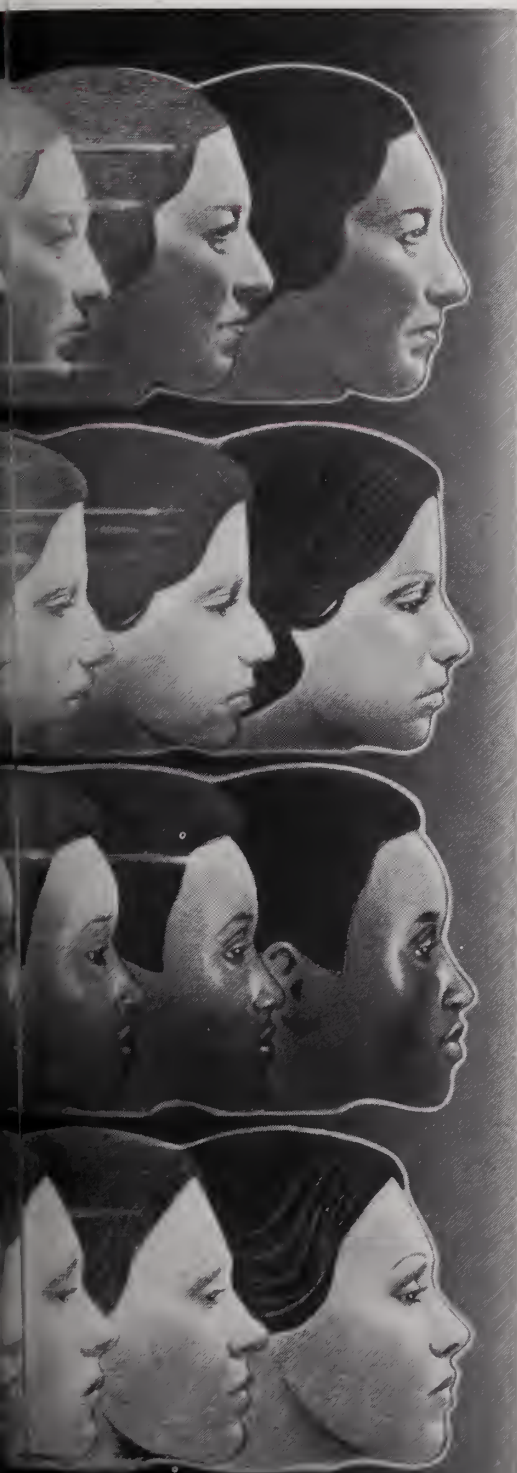
Each tablet contains:

**160 mg trimethoprim and 800 mg sulfamethoxazole  
in recurrent urinary tract infections  
due to susceptible organisms<sup>#</sup>**

<sup>#</sup>It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

Artist's conception of major uropathogens.

See next page for prescribing information.





Great taste  
means better  
compliance

**Maalox<sup>®</sup>**  
**Plus**

MAGNESIUM  
& ALUMINUM  
HYDROXIDES  
plus

**SIMETHICONE**  
**LEMON SWISS CREME FLAVOR**

The best  
tasting antacid  
you can  
recommend



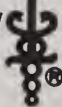
**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034

# Breast self-examination: KEY ROLE OF THE PHYSICIAN

<b>Item:</b>	Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.
<b>Item:</b>	Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, <i>fewer than 1 in 5</i> women practice BSE, and <i>only half</i> have an annual breast examination by a physician.
<b>item:</b>	Only 35% of all women polled reported that a <i>physician</i> had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.
<b>item:</b>	<i>But</i> , among women who received personal instruction from their physicians, the overwhelming majority (92%) practiced BSE during the preceding year.

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE. The American Cancer Society gives

major emphasis to breast cancer through research and a vast array of public educational materials, designed to give women life-saving information about the disease. Our latest approach is via a pioneering television film starring Jennifer O'Neill, "Breast Cancer: Where We Are." Where we *will* be in a few years will certainly hinge on our joint efforts.

**American Cancer Society** 

DORADO, 11 DE DICIEMBRE DE 1977  
EDUCACION MEDICA CONTINUADA

**SEMINARIO MEDICO**

**AUSPICIADO POR EL  
DEPARTAMENTO DE MEDICINA Y  
LA DIVISION DE EDUCACION  
MEDICA CONTINUADA  
ESCUELA DE MEDICINA, U.P.R.**

**CATEGORIA I - 4 CREDITOS**

**CONCEPTOS BASICOS Y  
MODERNOS EN LA TERAPIA DE LA  
HIPERTENSION ESENCIAL**

*Conferencias:*

- **EVALUACION DEL PACIENTE HIPERTENSO  
EN EL CONSULTORIO**
- **MECANISMO DE ACCION DE LAS DROGAS  
ANTIHIPERTENSIVAS**
- **TRATAMIENTO MEDICO DEL PACIENTE CON  
HIPERTENSION PRIMARIA**
- **USO DE NUEVOS AGENTES EFECTIVOS  
EN LA HIPERTENSION**

*Mesa Redonda:*

- **ASPECTOS PRACTICOS EN EL MANEJO  
DE LA HIPERTENSION**

*Conferenciantes:*

**MARIO R. GARCIA-PALMIERI, M.D.  
JOSE L. CANGIANO, M.D.  
FRANZ H. MESSERLI, M.D.  
RONALD OKUN, M.D.  
ELISEO C. PEREZ-STABLE, M.D.**

*Hotel Dorado Beach  
Dorado, Puerto Rico*

**Organizado por Pfizer Corporation**



# ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

JAN 16 1978

BOLETIN

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET



VOL. 69

Noviembre 1977

No.11

# A character all its own.



Valium (diazepam) is a benzodiazepine with a character all its own.

Pharmacologically, it has been described as more potent mg-per-mg than other available anxiolytic benzodiazepines. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> (diazepam)<sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.



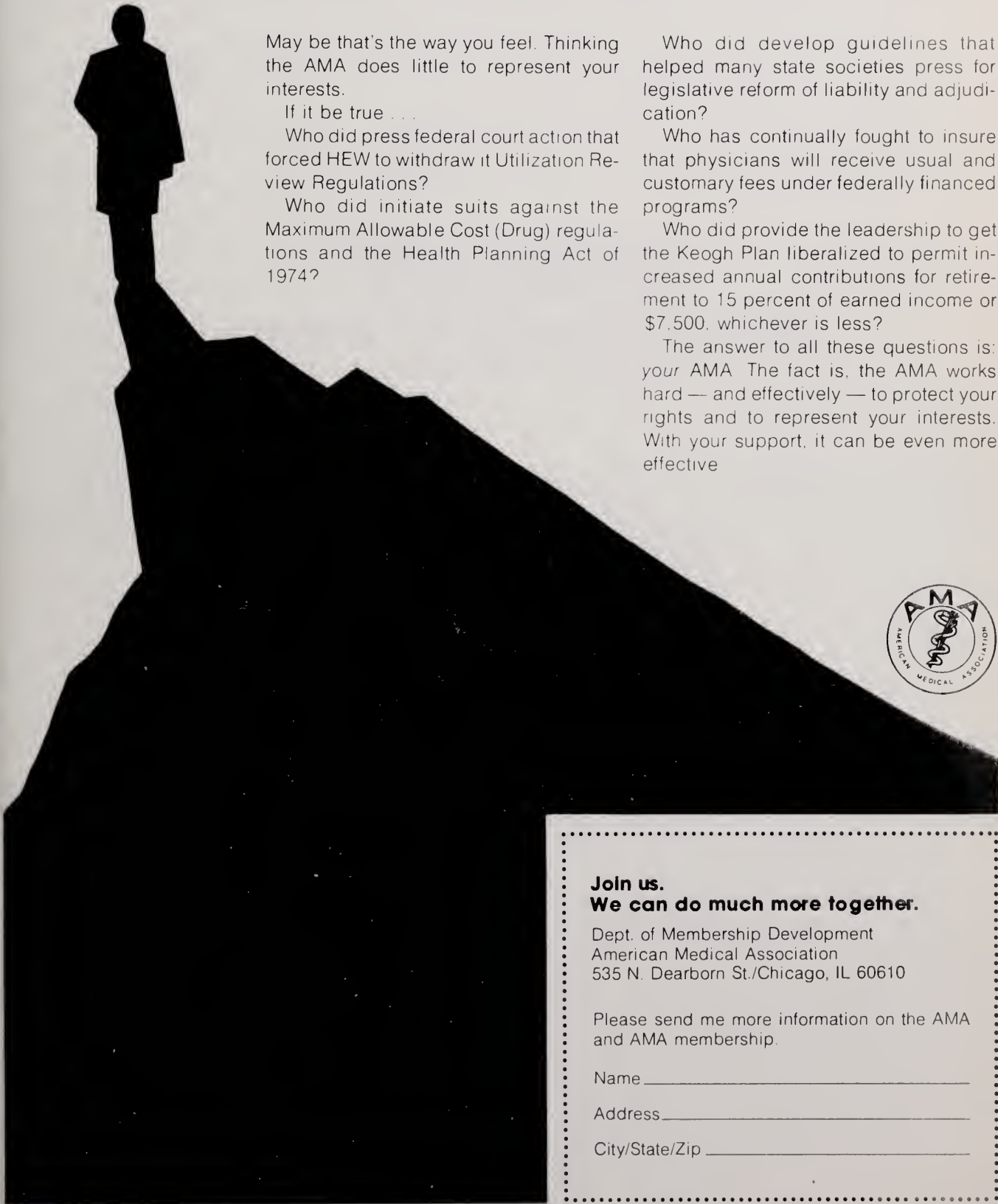
Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



# Quote: The AMA doesn't represent me. Unquote.

THE FRANCIS & TOWNSEND  
COPY OF MEDICINE  
BOSTON

JAN 16 1978



May be that's the way you feel. Thinking the AMA does little to represent your interests.

If it be true . . .

Who did press federal court action that forced HEW to withdraw its Utilization Review Regulations?

Who did initiate suits against the Maximum Allowable Cost (Drug) regulations and the Health Planning Act of 1974?

Who did develop guidelines that helped many state societies press for legislative reform of liability and adjudication?

Who has continually fought to insure that physicians will receive usual and customary fees under federally financed programs?

Who did provide the leadership to get the Keogh Plan liberalized to permit increased annual contributions for retirement to 15 percent of earned income or \$7,500, whichever is less?

The answer to all these questions is: *your* AMA. The fact is, the AMA works hard — and effectively — to protect your rights and to represent your interests. With your support, it can be even more effective.



**Join us.  
We can do much more together.**

Dept. of Membership Development  
American Medical Association  
535 N. Dearborn St./Chicago, IL 60610

Please send me more information on the AMA and AMA membership.

Name \_\_\_\_\_

Address \_\_\_\_\_

City/State/Zip \_\_\_\_\_



# THE ANXIETY-SPECIFIC.

- a predictable pattern of patient response
- seldom associated with serious side effects, in proper dosage
- rarely interferes with mental acuity
- used concomitantly with many primary medications
- three dosage strengths meet most patient needs

## LIBRIUM® chlordiazepoxide HCl/Roche 5mg, 10mg, 25mg capsules

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Relief of anxiety and tension occurring alone or accompanying various disease states.

**Contraindications:** Patients with known hypersensitivity to the drug.

**Warnings:** Caution patients about possible combined effects with alcohol and other CNS depressants. As with all CNS-acting drugs, caution patients against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psycho-

Libritabs® (chlordiazepoxide) available in 5 mg, 10 mg and 25 mg tablets.



tropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relation-

ship has not been established clinically.

**Adverse Reactions:** Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

**Usual Daily Dosage:** Individualize for maximum beneficial effects. **Oral—Adults:** Mild and moderate anxiety and tension, 5 or 10 mg *t.i.d.* or *q.i.d.*; severe states, 20 or 25 mg *t.i.d.* or *q.i.d.* **Geriatric patients:** 5 mg *b.i.d.* to *q.i.d.* (See Precautions.) **Supplied:** Librium® (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 100 and 500; Tel-E-Dose® packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Libritabs® (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100 and 500. With respect to clinical activity, capsules and tablets are indistinguishable.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

Please see following page.

# THE ANXIETY-SPECIFIC.

Since its discovery in the research laboratories at Roche, Librium has been the object of ongoing pharmacologic and clinical investigation.

The published record on Librium is enormous. So large, in fact, we put it into a computer literature retrieval system to make it more accessible in answering your inquiries.\*

It's a record that reveals a consistent pattern of patient response. A highly favorable benefits-to-risk ratio. And minimal interference with many primary medications.

Doing one thing well. Basically, that's what Librium is all about.

**LIBRIUM®**   
**chlordiazepoxide HCl/Roche**



**ROCHE**

If you have a question about Librium or any other Roche product, write to Professional Services, Roche Laboratories, Nutley, New Jersey 07110.

Please see preceding page for a summary of product information.



Organo Oficial

Fundado en 1903

Volumen 69

Noviembre 1977

Número 11

### JUNTA EDITORA

Jose I. Cangiano, Presidente; Juan M. Aranda, Ramon H. Bermúdez; José Juan Corcino; Herman J. Flax; F. Hernández Morales; Norman L. Maldonado; Manuel Martínez Maldonado; Francisco Olazábal; Osvaldo Ramírez Muxo, Carlos H. Ramírez Ronda; Nathan Rifkinson; Jesus M. Vázquez; Rafael Villavicencio Jiménez.

### SECRETARIO DE REDACCION

Sr. Gregorio Díaz

TODO MATERIAL SOMETIDO A ESTA PUBLICACION DEL BOLETIN DE LA ASOCIACION MEDICA DE PUERTO RICO PUEDE SER FOTOCOPIADO PARA PROPOSITOS EDUCACIONALES Y CIENTIFICOS NO COMERCIALES.

### Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725 6969.

### Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

### Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR cualquier relación con la política oficial es coincidencia.

Second Class postage paid at San Juan, P. R.

## CONTENIDO

Coronary Heart Disease - Sheehan's Syndrome .....	357
Charles D. Johnson, MD	
The Problem Drinker and Traffic Fatalities - Puerto Rico 1976 .....	364
Sidney Kaye, MSc, PhD	
Tétano: Patofisiología, Clínica, Tratamiento y Prevención .....	372
Héctor F. Gorbea, MD y Carlos H. Ramírez Ronda, MD, FACP	
Brief Communication: Temporary Arteritis .....	379
Víctor M. Mojica, MD, Alejandro Franco, MD and Radamés Sierra, MD	
Editorial: Dengue .....	381
Carlos A. Ramírez Ronda, MD, FACP	
Noticias .....	383

### NUESTRA PORTADA

In the heart of our small towns—  
the church, the plaza and  
the gracious balcony.

Cortesía de Banco Gubernamental de Fomento



# CORONARY HEART DISEASE IN SHEEHAN'S SYNDROME

Charles D. Johnson, MD

**Abstract:** Four cases of Sheehan's Syndrome believed associated with Atherosclerotic Heart Disease are described. This association has previously not been appreciated.

Atherosclerosis is stated to be characteristically absent in hypopituitarism (1), and there has been observed a lack of anginal symptoms even in male patients in an older age group (2). This article describes four patients with Sheehan's Syndrome who were believed to have coronary artery disease secondary to coronary atherosclerosis.

## Case Reports

### *Case 1:*

This 62-year-old female, gravida 7, para 3, abortion 4 was admitted to the hospital with a history of severe chest pain. Her last menses were at the age of 37 years, after her last pregnancy which was complicated by abortion and a large vaginal hemorrhage. Subsequently she lost libido, axillary and pubic hair, became weak, sluggish, pale and developed cold intolerance, constipation, headaches, low speech and mentation. There was no thyromegaly but the tongue was enlarged. The skin was dry, scaly and cold. There was a tremor and remote memory was impaired; a "Sheehan's habitus" was evident. The patient showed evidence of hypothyroidism, hypoadrenalism and hypo-

gonadism. A diagnosis of Sheehan's syndrome was made and cortisone acetate (one-half tablet daily) was begun about 11 years ago. Sodium levothyroxine was also taken until approximately two years prior to admission. There was a history of mild hypertension of 10 years duration but antihypertensive medications had been discontinued by the patient 9 months prior. There was no history of diabetes mellitus nor of cigarette smoking. The patient did well and there were no cardiac symptoms. Two sisters had hypertension and a brother had an unknown type of heart disease.

One week prior to admission she developed occasional rest chest pain lasting a few minutes and subsiding spontaneously. On the day of admission she developed severe oppressive retrosternal pain that radiated to the left arm, lasting for several hours, and accompanied by cold diaphoresis, nausea and dyspnea. The blood pressure was 130 systolic and 80 diastolic and the pulse 92 per minute, regular. Examination of the heart and lungs was negative, but there was loss of axillary hair and the skin was dry, cold and pale. All routine laboratory data were normal except for the following:  $\text{CO}_2$ -18 meg/l on one occasion; serum cholesterol-306, 318, 320 mg percent; LDH- 360, 450, 420 units ( $n = 100$ -225 units); SGOT - 99,121, 97 units ( $n = 10$ -50 units); CPK- greater than 1000 on two determinations and 850 units ( $n = 25$ -145 units/ml). The electrocardiogram revealed an acute anteroseptal myocardial infarction, a left axis deviation of -65 degrees, left anterior hemiblock, QRS complex widening (Figure 1), and a first degree A-V block on another tracing (not shown).

In the Coronary Care Unit the patient was given cortisone acetate, 25 mg p.o. daily. She suffered several episodes of moderately severe chest pain relieved by meperidine. Five days later she developed severe chest pain and cold sweating, treated with meperidine, phenergan, cortisone acetate-50 mg IM and hydrocortisone sodium succinate 20 mg IV. The pain continued and

---

*From the University of Puerto Rico School of Medicine, Department of Medicine, Section of Cardiology, Río Piedras, P. R. 00936.*

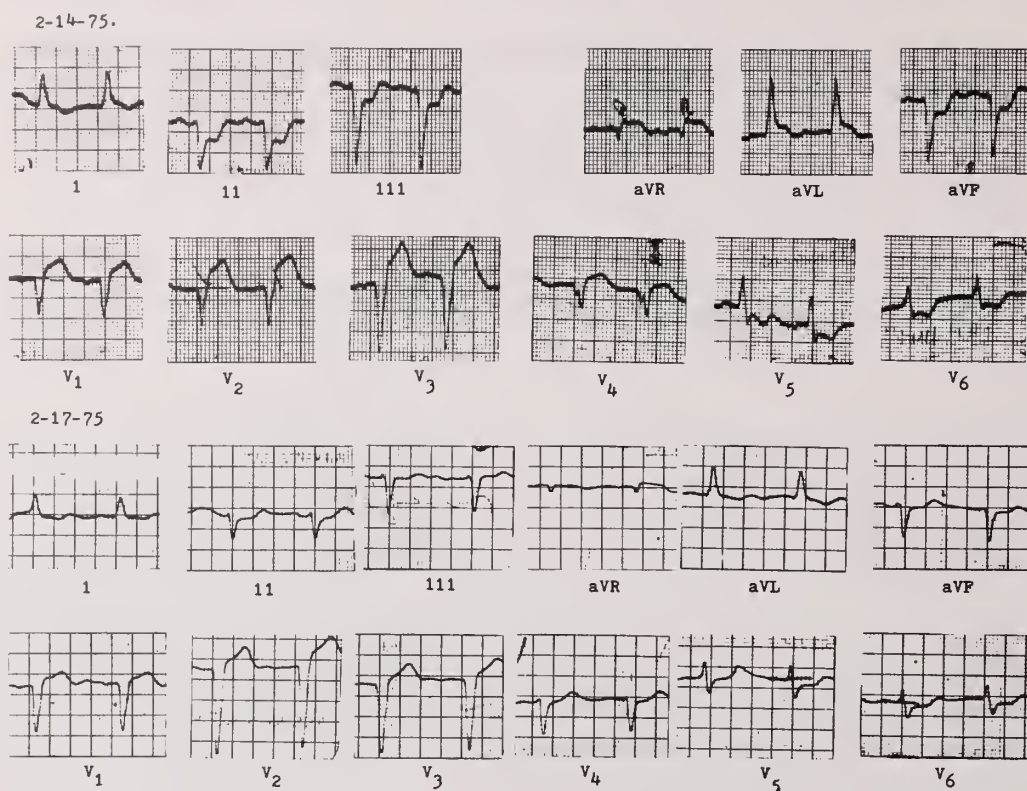


Fig. 1 - Case 1: Acute antero-septal myocardial infarction. Left axis deviation of  $-65$  degrees. Left anterior hemiblock, with QRS complex widening.

cardiorespiratory arrest ensued, followed by death.

Autopsy examination revealed cardiomegaly, the heart weighing 430 grams and the left ventricle measuring 1.9 cm (concentric type). The coronary arteries revealed 90 percent obstruction with severe atherosclerosis, an acute antero-septal infarction with anterior and anterolateral scarring. The right and left coronary arteries were partially occluded by multiple atheromatous plaques; multiple atheromatous plaques were seen in the base of the mitral valve. Microscopic examination revealed ischemic changes, from recent up to 72 hours of age (Figure 3). Severe grade IV aortic atherosclerosis with ulcerations in plaques was present. There was absence of axillary and pubic hair. The breasts were small and firm. The endocrine glands were small and showed trophic changes and fibrosis. The pituitary gland showed marked fibrosis and the adrenals severe cortical atrophy; the thyroid gland and the ovaries were markedly fibrotic, and the uterus showed cystic degeneration. Death was due to acute myocardial infarction.

#### Case 2:

This 61-year-old female with Sheehan's syndrome and diabetes mellitus was taking cortisone acetate-12.5 mg twice daily and sodium levothyroxine-0.2 mg daily, and was doing well until the time of her myocardial infarction, at which time she developed severe chest pain, sweating, dyspnea and anxiety. At the time of hospital admission she was noted to be obese, hoarse, pale, with coarse and dry skin and to be "fully hypothyroid". The blood pressures were 160 and 136 systolic, and 100 and 84 diastolic, respectively. Cardiomegaly, an atrial gallop and congestive heart failure were observed. Remarkable laboratory data were an alkaline phosphatase of 225 mu/ml ( $n = 30-85$  mu/ml), a serum cholesterol of 240 mg percent, total lipids of 310 mg percent, fasting blood sugars ranging from 120 to 200 mg percent and elevated LDH, SGOT and CPK enzymes. The electrocardiograms revealed an acute antero-septal myocardial infarction, a left axis deviation of  $-30$  degrees, a borderline left anterior hemiblock (Figure 2), and premature ventricular contractions (not shown).

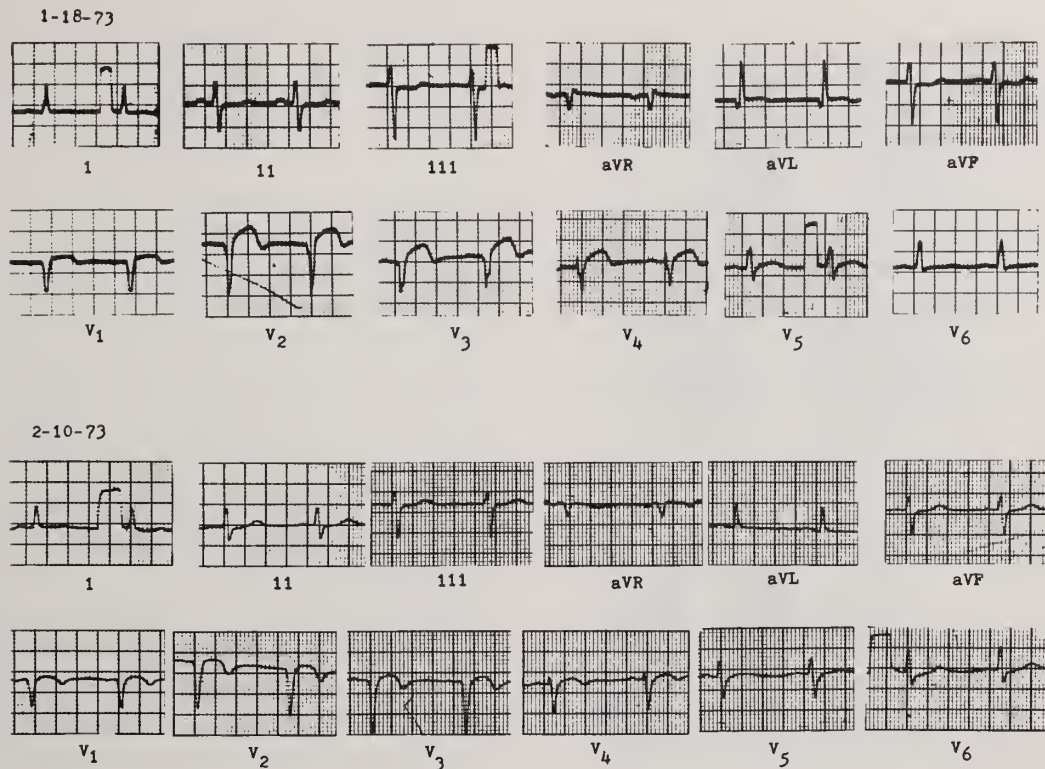


Fig. 2 - Case 2: Acute anteroseptal-lateral myocardial infarction. Left axis deviation of  $-30$  degrees. Border-line left anterior hemiblock.

Therapy consisted of bed rest, analgesics, digitalis, diuretics, NPH insulin, cortisone acetate-12.5 mg twice daily and sodium levothyroxine -0.1 mg daily. Diagnoses were atherosclerotic heart disease, acute myocardial infarction, Sheehan's syndrome, diabetes mellitus and hypertension.

#### Case 3:

A 51-year-old female who at the age of 29 years developed profuse vaginal hemorrhage in the seventh month of gestation, requiring three blood transfusions and Caesarean section with sterilization. In the subsequent years, beginning one year later, she noted falling of the hair, decreased menses and libido, poor appetite, sluggishness, polydipsia, polyuria, swelling of the face and hands, and a dry, wrinkled, puffy skin. Acute pyelonephritis occurred. Sheehan's syndrome was diagnosed at the age of 36 years.

Four years later pyelonephritis recurred, and the electrocardiogram showed ST segment and T wave changes. At age 42 years systemic hypertension (systolic

pressures of 140 to 180 mm Hg and diastolic pressures of 100 to 140 mm Hg, respectively), left ventricular hypertrophy and strain were detected, and cortisone acetate and sodium levothyroxine were prescribed. No cardiac diagnoses were entertained until age 44 when she developed precordial pain, palpitations, dizziness, sweating, dyspnea, orthopnea and leg edema, and she was believed to have atherosclerotic heart disease and a myocardial infarction; SGOT enzymes ranged from 18 to 69 units. The following year she had severe anginal and retrosternal pain. Gastroenteritis and acute adrenal insufficiency occurred. Hypothyroidism was evident. A grade II systolic murmur along the left sternal border and at the heart base has been observed, as well as a xanthelasma. Angina pectoris and marked chest pain with elevated enzymes believed to be myocardial infarction and pre-infarction syndrome have occurred on subsequent occasions. Recently she suffered severe retrosternal chest pain that radiated to the neck and left arm, associated with cold sweating, nausea, dizziness and dyspnea; the



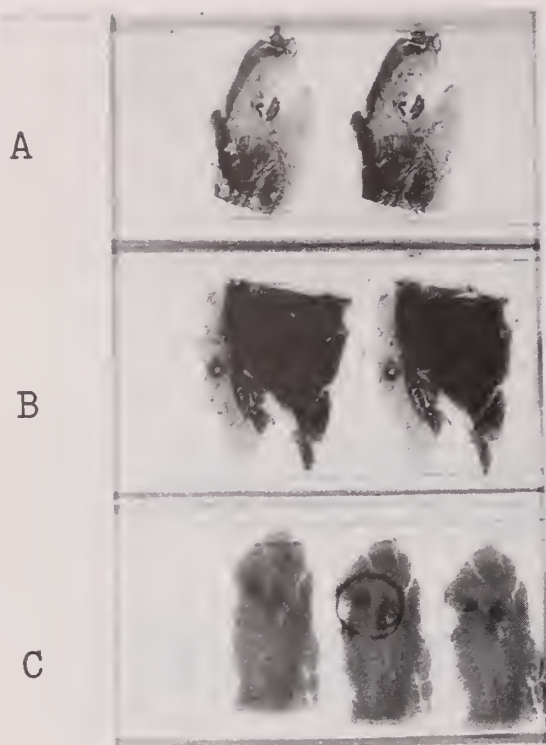


Fig. 3 - Case 1: A and B. Panoramic microscopic views of coronary arteries showing atherosclerosis and plaques. C. Microscopic views of heart muscle showing necrosis.

pain was not relieved by nitroglycerine. The ECG remained "unchanged", but the serum enzymes were as follows: SGOT-90, 62,75; LDH-190,310,245; CPK-190,160. Serum cholesterol was 325-330 mg percent.

Again recently, during a urinary tract and upper respiratory tract infection the patient developed adrenal crisis. During latter years almost all blood pressures have been elevated, as high as 180 systolic and 125 mm Hg diastolic and the electrocardiograms persistently show marked left ventricular hypertrophy and strain but no definite signs of infarction (q wave in lead I, Q in a VL). Therapy has consisted of cortisone acetate-37.5 mg daily, sodium levothyroxine, alphamethyldopa, digitalis, diuretics, isosorbide dinitrate and nitroglycerin. The diagnoses of Sheehan's syndrome and moderately severe systemic hypertension are well-accepted in this patient. She has had chest pain on many occasions and is believed to have ischemic heart disease, anginal pain and

probably she has suffered at least two myocardial infarctions, although the data do not confirm this definitely.

#### Case 4:

A 63-year-old female whose fifth pregnancy was complicated by profuse vaginal bleeding and loss of consciousness after a home delivery. Subsequently she failed to lactate and one year later the menses decreased and amenorrhea ensued. A diagnosis of Sheehan's syndrome with hypothyroidism has been appreciated for at least 13 years, and she has received cortisone acetate-25 mg and sodium levothyroxine-0.2 mg daily. There is a four-year history of hypertension. There is a history of hypertension and chest pain in her family. For the past five years she has suffered recurrent chest pains requiring hospitalizations. Pre-infarctional angina was believed to be present. Congestive heart failure occurred. Electrocardiograms have been normal except for slight ST segment sagging in leads aVF and V<sub>3-6</sub>. Last year she developed a urinary tract infection associated with an acute adrenal crisis. Blood pressures ranged from 110 to 180 systolic and from 60 to 80 mm Hg diastolic, respectively. The thyroid gland was not palpable, but body hair was decreased and no pubic hair was present. *Klebsiella* and *Pseudomonas* organisms were cultured from the urine. Serum cholesterol was 184 mg percent. Serum LDH, SGOT and CPK enzymes were normal.

The electrocardiograms were normal, or showed only nonspecific ST segment and T wave abnormalities compatible with digitalis effect.

Therapy consisted of cortisone acetate, hydrocortisone sodium succinate, sodium levothyroxine (discontinued temporarily because of the development of chest pain) and digitalis. The patient continued having angina pectoris, mostly with stress and relieved by nitroglycerin. She was subsequently discharged on digitalis, isosorbide dinitrate, cortisone acetate and sodium levothyroxine. The diagnosis of angina pectoris secondary to atherosclerotic heart disease was accepted.

#### Discussion

It has been stated that atherosclerosis and coronary disease are characteristically absent in hypopituitarism (1). The lack of anginal symptoms even in male patients in an age group above 60 was believed to indicate that long-lasting hy-

popituitarism, despite hypercholesterolemia, does not lead to coronary disease as expected (2). A possible explanation suspected is that these patients work little, are slow and inactive, sleep much, are apathetic and inexcitable, have no sexual activity, and thus this manner of life protects them from myocardial infarctions (2). In general, the clinical course of hypopituitary patients is not marked by cardiac disorders (3).

However, this characteristic absence of atherosclerosis in hypopituitarism may not necessarily be a fact, particularly in the patient who is maintained on replacement therapy.

In Sheehan's original classic report he observed cardiovascular changes, including atheroma, in the coronary arteries, abdominal and cerebral vessels, and in the majority of cases there was a moderate degree of aortic atheroma. These included a 34-year-old female with mitral and tricuspid stenosis, a 69-year-old female, and a 68-year-old male with a pituitary cholesterol cyst who had had cardiac symptoms, and collapsed suddenly and expired; his heart weighed 600 grams (the mean heart weight in the total group was 207 grams) and demonstrated old and recent infarcts due to coronary atheroma; there were hypertensive changes of the renal arterioles (4).

In Wilson's seven cases of pituitary insufficiency in women (four with Sheehan's syndrome), there was a high incidence of arterial disease. Of the four Sheehan patients, two suffered intermittent claudication in the calves, one had a myocardial infarction, and three had angina pectoris; the angina of one patient increased with thyroid extract (5). The authors of another study noted that it remained unanswered if anterior pituitary insufficiency predisposed to coronary artery disease, although the possibility of a causal relationship had been previously mentioned. Of their 22 patients with hypopituitarism of pregnancy, followed for as long as 25 years, none demonstrated clinical evidence of cardiac insufficiency, and only two patients developed vascular disease - one had mild hypertension and the other had probable

electrocardiographic signs of coronary artery disease (Q waves in leads 111 and aVF). Two cases showed early retinal arteriosclerosis (6).

Del Castillo and associates noted angina in two of six patients at an age younger than would be expected in females (7). One of Moszkowski's five postpartum pituitary insufficiency patients, a 39-year-old female (his Case 4), suffered angina pectoris and a myocardial infarction. She had been on replacement therapy of hydrocortisone, 20 mg daily, and thyroid, 32 mg daily (8).

Albeaux-Fernet et al observed the unusual course of a case of typical Sheehan's Syndrome who developed severe hypertension, severe coronary pain and finally stenosis of the right renal artery associated with severe atheroma, which had not previously been seen in this form of hypopituitarism (9).

Hypertension is a major risk factor in the causation of atherosclerosis. Adrenal cortical hypofunction is associated with hypotension, and it has been stated that this prevents the development of hypertension and the atherogenesis of hypothyroidism in hypopituitarism, so that patients are immune to diseases which mostly damage the heart in adults (2). However, in Sheehan's patients the blood pressures were labile, either low or high, and fell during an Insulin Tolerance Test (4). All four of the patients in the present report had hypertension at some time in their course, but only Case 3 had significantly severe hypertension.

Hypercholesterolemia is another major risk factor for coronary heart disease. Cholesterol and lipids are usually above normal (250-300 mg percent) in hypopituitarism, but fluctuate, and may even be subnormal (3, 4, 10, 11). Two cases (Cases 1 and 3) of this group showed elevated cholesterol values.

Diabetes mellitus is associated with early, frequent and severe coronary atherosclerosis (12, 13). Case 2 had diabetes mellitus.

Pituitary insufficiency may produce cardiac changes similar to those of myxedema or of Addison's disease. Brown atrophy and dege-



neration of muscle fibers are characteristic. The blood pressure is often low and heart size small, although both may be normal. Localized areas of myocardial necrosis, fibrosis and degeneration occur in Addison's disease. An Addisonian crisis has simulated a myocardial infarction, but these are uncommon in hypopituitarism (1, 13).

The association of atherosclerosis with primary myxedema is controversial, but pathological and clinical evidence of atherosclerosis appears earlier and of greater frequency and intensity. Myocardial infarctions are common and the coronary sclerosis is usually not reversible (13, 14, 15, 16). A low titer of thyroid antibody with minimal asymptomatic atrophic thyroiditis (premyxedema) causing hypercholesteremia lasting for many years may favor the development of coronary atherosclerosis and myocardial infarction, especially in women. Coronary artery disease was common (52 percent with degenerative disease) in these patients and their relatives (17, 18, 19). High TSH (not present in Sheehan's Syndrome) has been suspected to have a role in atherogenesis. Other authorities believe that there is only suggestive evidence that the hypercholesteremia and lipid abnormalities associated with myxedema predispose the female to premature advanced coronary atherosclerosis and increase the incidence of coronary artery disease in the male (14). Also, hypertension is common in myxedema. The coronary atherosclerosis may be asymptomatic until thyroid therapy is initiated, when coronary insufficiency may become unmasked from the increased metabolism; but both angina pectoris uncommonly and myocardial infarction can occur in myxedematous patients prior to thyroid hormone therapy. Angina may actually improve with thyroid therapy. In some patients with hypothyroidism the coronary arteries are normal (1, 13). The enzymes of CPK, SGOT and LDH may be increased in hypothyroidism alone (14).

Various cardiovascular and electrocardiographic abnormalities have been described in

diseases of the pituitary, both in acromegaly (20) and in hypopituitarism (1, 2, 4, 6, 13, 21). Changes observed in the latter comprise generalized low QRS voltage, bradycardia infrequently, small P waves, left axis deviation rarely, ST segment depression in the left precordial leads. Q-T interval prolongation, low, inverted or flattened T waves in all standard and precordial leads, a slightly prolonged mean P-R interval and unusually a first degree atrio-ventricular block. The changes of myxedema may predominate (however, ST segment depression and Q-T interval prolongation are rare), or the findings may be those of adrenal cortical hypofunction (in which T wave abnormalities are rare). Adequate hormonal therapy reverses all these abnormalities. Thyroid may correct the low voltage; cortisone alone may reverse the ST-T and Q-T abnormalities. However, both drugs are necessary in some patients, especially in pituitary hypothyroidism. In primary hypothyroidism, thyroid alone can induce dramatic electrocardiographic response (1, 6, 21).

All patients in this study were on replacement therapy at the time of the myocardial infarction or angina pectoris, except in Case 1 the sodium levothyroxine had been discontinued about two years prior. Even rarely, pregnancy has occurred in patients with antecedent Sheehan's Syndrome. Estrogen and cortisone therapy may have influenced pituitary-adrenal function in two cases (22).

Thus, these four cases of Sheehan's Syndrome are believed to have coronary heart disease on the basis of coronary atherosclerosis. Two of the cases demonstrated typical infarction electrocardiograms, and myocardial infarction was proven in one at autopsy. The other two cases are considered to belong to the atherosclerotic heart disease spectrum on the basis of clinical evidence.

### Acknowledgments

The author wishes to thank J. Ortega Gil, MD, for his help in securing the patients; Eduardo de León, MD, Chief of Pathology, for his interpretation of the pathological mater-



ial. The patients were followed by the Section of Endocrinology, UPR School of Medicine.

## References

1. Wenger, N. K., Herndon, E. G.: Endocrine and metabolic disorders, Chap 82, in *The Heart*, edited by Hurst, J. W. 3rd Ed. New York, McGraw-Hill, 1974, p. 1484, 1490.
2. Kosowicz, J., Roguska, J.: Electrocardiogram in hypopituitarism. Reversibility of changes during treatment. *Am Heart J* 65: 17-23, 1963.
3. Aloia, J. F., Field, R. A.: The heart and the endocrine system, chap. 47, in *Cardiac and Vascular Diseases*, edited by Conn, H. L., Horwitz, O. Philadelphia, Lea & Febiger, 1971, p. 1261-1263.
4. Sheehan, H. L., Summers, V. K.: The syndrome of hypopituitarism. *Quart J Med* 18: 319-378, 1949.
5. Wilson, L. A.: Pituitary insufficiency in women. A clinical study of seven cases. *Lancet* 1: 203-207, 1953.
6. Bernart, W. F., de Andino, A. M.: Electrocardiographic changes in hypopituitarism of pregnancy. *Am Heart J* 55: 231-238, 1958.
7. Del Castillo, E. B., Scharer, R. F., Guardo, A. H., et al: Considerations a propos de quelques troubles cardiaques au cours du syndrome de Simmonds-Sheehan. *La Presse Medicale* 11: 806-807, 1963.
8. Moszkowski, E. F.: Postpartum pituitary insufficiency. Report of five unusual cases with long-term follow-up. *South Med J* 66: 878-882, 1973.
9. Albeaux-Fernet, M., Gelinet, M., Deribreux, J.: Sheehan's disease followed by severe arterial hypertension with right renal artery stenosis. Discussion of the role of hypopituitarism in atherogenesis. *Sem Hop Paris* 49: 261-265, 1973.
10. Jacobs, D. R., Krieger, D. T., Charles, R. N.: Late appearance of hyperlipemia in hypopituitarism. *Ann Intern Med* 55: 640-646, 1961.
11. Summers, V. K., Hipkin, L. J., Davis, J. C.: Serum lipids in diseases of the pituitary. *Metabolism* 16: 1106-1113, 1967.
12. Digirolamo, M., Schlant, R. C.: Etiology of coronary atherosclerosis, Chap. 48, in *The Heart*, edited by Hurst, J. W. 3rd Ed. New York, McGraw-Hill, 1974, p. 991.
13. Friedberg, C. K.: Diseases of The Heart, 3rd Ed., Philadelphia, W. B. Saunders Co., 1966, p. 646, 716, 874, 1630, 1635-36, 1642-43, 1653, 1662-63.
14. Ingbar, S. H., Woeber, K. A.: The thyroid gland, chap. 4, in *Textbook of Endocrinology*, edited by Williams, R. A. 5th Ed. Philadelphia, W. B. Saunders Co., 1974, p. 143, 193.
15. Steinberg, A. D.: Myxedema and coronary artery disease - A comparative autopsy study. *Ann Intern Med* 68: 338-344, 1968.
16. Blumgart, H. L., Freedberg, A. S., Kurland, G. S.: Hypercholesterolemia, myxedema, and atherosclerosis. *Am J Med* 14: 665, 1953.
17. Vanhaelst, L., Neve, P., Chailly, P., et al: Coronary artery disease in hypothyroidism. *Lancet* 2: 800-802, 1967.
18. Basteine, P. A., Vanhaelst, L., Neve, P.: Coronary artery disease in hypothyroidism. Observations in preclinical myxoedema. *Lancet* 2: 1221-1222, 1967.
19. Fowler, P. B. S., Swale, J., Andrews, H.: Hypercholesteremia in borderline hypothyroidism. Stage of premyxoedema. *Lancet* 2: 488-491, 1970.
20. McGuffin, W. L., Sherman, B. M., Roth, J., et al: Acromegaly and cardiovascular disorders. *Ann Intern Med* 81: 11-18, 1974.
21. Stephan, E., Laham, E., Panier, M., et al: Coeur et hypopituitarisme. *Arch Mal Coeur* 58: 1493-1502, 1965.
22. Jackson, I. M. D., Whyte, W. G., Garrey, M. M.: Pituitary function following uncomplicated pregnancy in Sheehan's syndrome. *J Clin Endoc & Metab* 29: 315-318, 1969.
23. Sheehan, H. L., Davis, J. C.: Pituitary necrosis. *Br Med Bull* 24: 59-70, 1968.

# THE PROBLEM DRINKER AND TRAFFIC FATALITIES IN PUERTO RICO — 1976

Sidney Kaye, MSc, PhD

## Summary:

### Over all traffic fatalities:

- 1) Traffic fatalities appears to be stabilized in Puerto Rico; but 500 deaths a year is still a horrible situation to accept.
- 2) Pedestrians traffic fatalities *still* outnumber driver deaths 2 to 1.
- 3) Males outnumber females 4 to 1 (about the same as for 1968-1975).
- 4) Pedestrians M to F (4 to 1); age most represented was 51-60 years (in 1975 it was 60-70 yrs).
- 5) Driver M to F (21:1); age most represented was again 21-30 years.
- 6) Mostly occurred during the evening of the week-end.

### Alcohol Related:

- 1) Males by far outnumbered female by 25:1; in 1975 it was 26:1.
- 2) Driver: 80 tested; 19 positive (18M: 1F) 61 percent positive.
- 3) Pedestrian: 108 tested; 17 positive (15M:1F) 11 percent.
- 4) The week-end (Sat-Sund-Frid) outnumbered the rest of the week by 2 to 1. Saturday represented 1/3; Saturday and Sunday - 1/2.
- 5) 78 percent were above 0.10 gm/dl (heavy drinking) (71 percent in

1975). 62 percent were above 0.15 gm/dl (very heavy drinking) (50 percent in 1975). It is the problem (heavy) drinker who represents only 10 percent of our total drinkers - who is in fact causing most of these fatalities. This is in agreement with previous years (1968-1975).

- 6) Teenagers (15-20) increasing involvement with traffic fatalities and alcohol is alarming. The permissiveness and relief of some parents toward rising juvenile alcoholism rate as a substitute for the "hard drugs" is very disheartening. The teenage drinking has risen sharply in the United States and is slowly beginning to rise here in Puerto Rico. White rum has become extremely popular in the United States among the teenagers; and here we have plenty of it available. The future does not look good for our youths unless this trend is stopped. The first corrective step *must* be taken at home.

The killing on our highways still goes on in spite of special efforts by state and federal agencies. In the United States there are about 50,000 traffic fatalities per year (this is more than was killed in the Korean War); and here in Puerto Rico we have about 500 per year (509 for 1976). See Table I.

These numbers mean nothing to you or me — because we really believe that it can't happen to us! Just like the slogan "Don't drink and then drive" is also meaningless to us in spite of

TABLE I  
Deaths on our Highways (1-10)

USA	YEAR	PR
54,862	1968	545
55,791	1969	542
54,800	1970	451
54,200	1971	478
56,600	1972	552
55,600	1973	577
46,200	1974	565
45,600 *	1975	503
47,100	1976	509

\* - The increase in price of gasoline and the 55 miles speed limit went into effect.

the fact that we should know better.

In our traffic fatalities we have found by our studies since 1963 (1-10) that alcohol was the most frequent common denominator. This is no surprise since about 1/2 of our adult population use the highway (at least occasionally) after drinking; what (if anything) can we do about it? Prohibition cannot work; it did not work in 1917-1932. Nothing will work without popular acceptance.

But somehow we will have to change our general attitude about drinking. This will not be easy because most drivers believe that they are good drivers even after having a "few", and that they are social drinkers who rarely get drunk.

Little does he know that 1 in every 10 social drinkers is a problem drinker (11).

Also that anyone who just *has to have* that drink now; or one who does not know when to start and when to stop; *and* one who drinks more than 3 or 4 or 5 "shots" within a relatively short interval — *is no social drinker*.

The tragic fallacy to "I'm not drunk" and I can drive OK — is that you don't have to be "obviously drunk" to be an unsafe driver (12).

Slurred speech, incoordination, staggering

gait are the signs of marked intoxication (13).

The more subtle central nervous system depressant action on judgement, concentration, prudence, vision, reaction time and coordination which are so vital to our ability to respond to an emergency situation and to "safe driving" — can be effected with even *small* amounts of alcohol.

It is not easy to convince a drinking man that at a blood alcohol concentration (BAC) of 0.10 gm/dl he is 7 times more apt to have an accident; and at 0.15 gm/dl this goes to 28 times.

How many drinks does it take to reach a 0.10 gm/dl; — at least 6 oz of 80 proof (within a 2 hour interval) for a 160 lb. person (14).

The legal-limit now set by all 50 states and Puerto Rico is 0.10 gm/dl BAC.

In the United States during the 1950's, 1 out of 3 driver fatalities were positive for alcohol; in the 1960's it went to 2 in 5 and then to 50 percent or better (14).

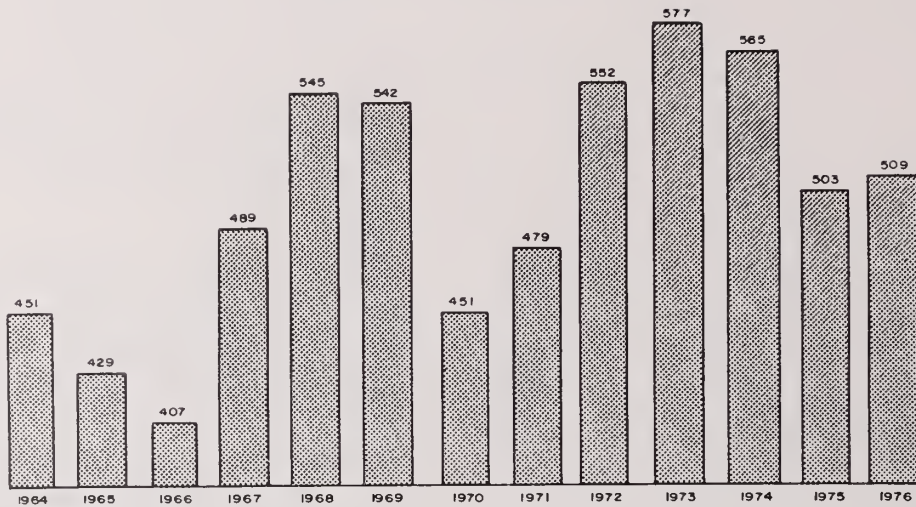
In Puerto Rico we are world famous for our excellent rum, and we annually produce more than 50 million gallons of which 5 is kept for local consumption; the rest is exported. This is a lot of local consumption for a 3.2 million population with about 1.8 million over 16 years of age. When compared with other countries in total alcohol consumption of distilled spirits plus wines and beer, Puerto Rico ranks 10th. But if we consider the per capita consumption of distilled spirits alone, Puerto Rico ranks first in the world followed by France and the United States (15). This is a very dubious distinction.

With this background, let us now look at our data on the involvement of the problem drinker in traffic fatalities in Puerto Rico during 1976.

#### Statistical Data 1976

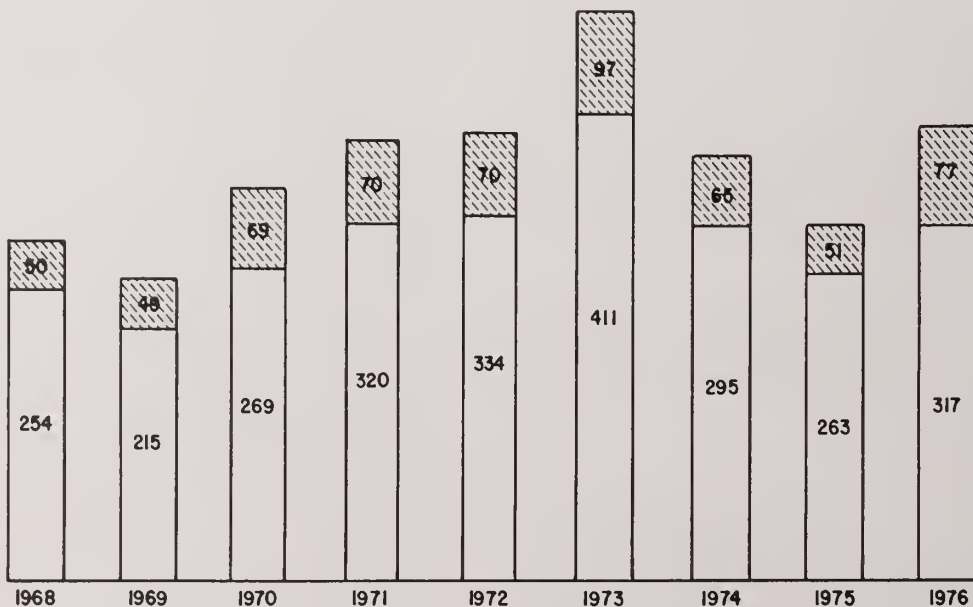
In Puerto Rico (100 miles x 35 miles) with



DEATHS ON HIGHWAY IN PUERTO RICO  
1964-1976

POST-MORTEM EXAMINATION OF TRAFFIC DEATHS BY SEX 1968-1976

 FEMALE  
 MALE



a population of about 3.2 million persons (16); 814, 323 registered vehicles; 859,642 drivers, there are 12,273.2 kilometer of highway; and on these highways there were 85,813 traffic accidents that resulted in approximately 33,472 personal injuries and 509 traffic deaths (16, 17).

Of the total 509 traffic deaths, we were able to study in some measure 394 cases that were submitted for blood alcohol levels following an autopsy. Of these, 311 were autopsied at the Institute of Legal Medicine (School of Medicine) of the University of Puerto Rico.

and 22 from Mayaguez Medical Center.

The 394 traffic fatalities that were studied, were separated and categorized as to pedestrian, driver, passenger, age, sex, occupation, and day of week. Only those persons over 15 years old, and those who died within 5 hours of the accident were analyzed for (presence and amount) of alcohol in the blood.

With this data assembled, it was again shown that males outnumber females 4:1 (317M - 80 percent and 77F - 20 percent). This follows the same general trend as in 1975 when it was 5:1.

In Puerto Rico, the pedestrian continues as in previous years to account for the majority of our traffic deaths studied. This year the pedestrians accounted for 193 cases (150M - 78 percent and 43F - 22 percent); or 49 percent of the total 394 cases studied. This is in sharp contrast to the drivers who accounted for 25 percent (99) of the total traffic deaths studied. In this group there were 95 males and 4 females. In ratio, the males by far outnumber the female by about 24 to 1 in the fatal "driver" category.

The passengers accounted for 15 percent (59 cases; 39M:20F). The remaining 43 cases were: 5 motorcyclists, 4 bicyclists, one horseman, and in 33 cases the categories were not clearly established.

## Pedestrian

As in the years 1968, through 1975; and again in 1976, the pedestrian contributed by far to the majority of our traffic deaths. All ages totalled 193 (150M:43F). The largest representative age group was between 51-60 years, with 40 cases (33M:7F).

The occupation of the pedestrians studied fell into these categories: First laborers, next students and next housewives.

## Driver

Drivers accounted for 99 highway deaths

POST MORTEM EXAMINATION BY CATEGORIES  
 1976

ALL EXAMINATIONS = 100%

PEDESTRIANS 49% (193)

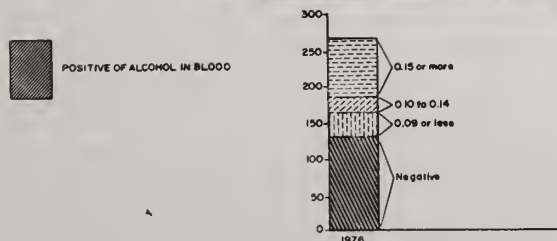
DRIVERS 25% (99)

PASSENGERS 15% (59)

OTHERS 8% (33)

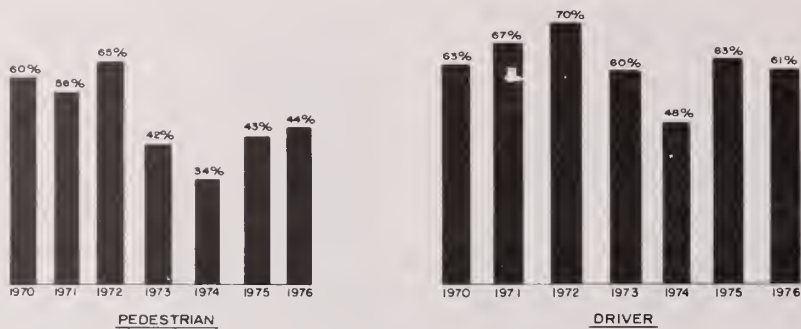
ALCOHOL SAMPLES OF POST-MORTEM EXAMINATIONS  
 1976

of the total of 267  
 traffic fatalities  
 tested for alcohol  
 in blood

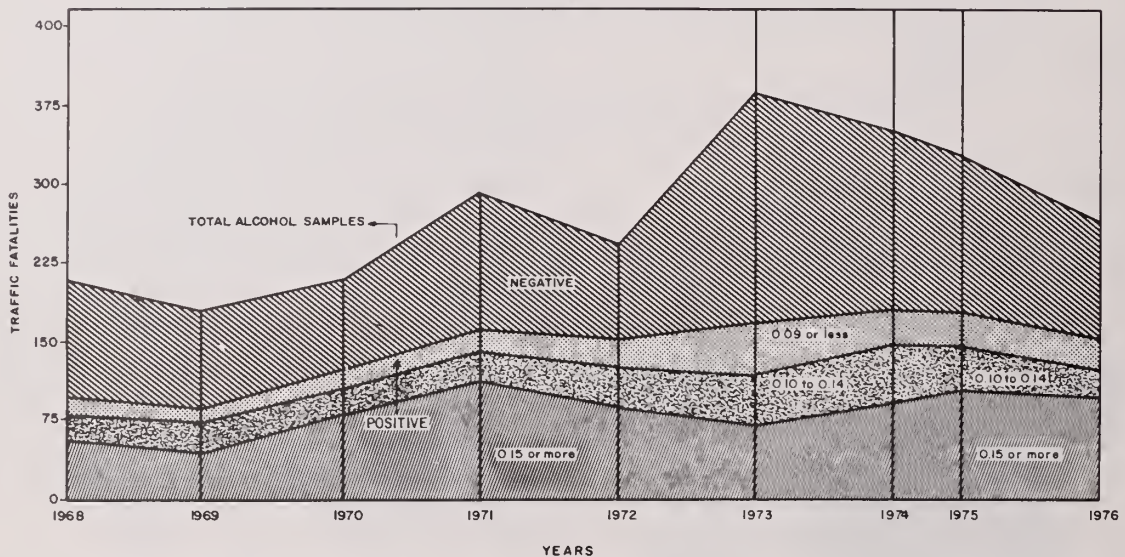


The remainder 83 specimens were sent from the rest of the Island; 47 from the Arecibo District Hospital, 9 from the Fajardo District Hospital; 5 from the Ponce District Hospital;

PERCENTAGE OF POSITIVE ALCOHOL OF DRIVERS  
AND PEDESTRIAN TESTED 1970-1976



ALCOHOL SAMPLES OF TRAFFIC DEATHS BY PERCENT OF ALCOHOL IN BLOOD  
1968-1976



or 25 percent of the total studied. There were only 4 females to 95 males (1:24). The age group that contributed the most fatalities was 21-30 years with 33 deaths (31M:2F). Males by far outnumber females. As to occupation of these drivers, laborers were first, with merchants next, and students next.

#### Passenger

The passengers accounted for 15 percent (59 cases; 39M:20F). The remaining 43 cases were: 5 motorcyclists, 4 bicyclists, 1 horseman, and in 33 cases the categories were

not clearly established.

#### Day of Fatal Traffic Accident

The distribution of the fatal cases by day of week occurrence, again shows that most deaths occurred during Sunday, Saturday and Friday with 196 cases (163M:33F) 50 percent out of the total of 394. Of these 196 cases, 163 were males and 33 were females. Monday follows with 43 cases; Wednesday with 42; Thursday with 40, and Tuesday with 34 cases. There were 39 cases where the day of the accident was not clearly established.



### Positive Blood Alcohol Concentration

In 267 cases of the total of 394 post-mortem examination, blood alcohol levels were determined. In the remaining 127 cases, no blood alcohol was determined because of the long interval of time elapsed between the accident and the death; also no blood alcohol was determined on persons under 15 years old.

Of the total of 267 cases analyzed for blood alcohol content, 134 (50 percent) were positive; 129 males and 5 females, in a proportion of males over females of 26:1. The remaining 133 (50 percent) cases were alcohol negative in the blood sample of which 98 were males and 35 were females.

When we distributed the 134 positive cases by categories, such as: Pedestrians, drivers, passengers, etc., we found that 47 cases were pedestrians, 45 males and 2 females. This represented 35 percent of the total of 134 positive alcohol cases and 44 percent of all pedestrians tested (108). Next were the drivers with 49 positive alcohol cases (48 males and only one female). This is 37 percent of the total positive alcohol cases and 61 percent of the total drivers tested (80). The passengers follows with 14 positive alcohol cases of this (13 males and 1 female). This is 10 percent of the total positive alcohol cases and 24 percent of the total passengers tested. The motorcyclist contributed with 5 cases of which 2 were positive for alcohol, and in 33 cases the categories were not established but contributed with 22 cases positive for alcohol.

### Positive BAC and Day of the Week

The total positive cases were separated by day of the week. This separation demonstrated that Sunday accounted for the largest number of positive alcohol cases with 36 (27 percent), then followed by Saturday with 31 (23 percent) then Friday with 18 cases (13 percent).

In other words, these three days accounted for 85 cases (63 percent) positive alcohol cases of the total of 134. The remaining 49 cases were distributed in the remaining days of the week, that is: Monday with 11 cases; Tuesday with 8 cases; Wednesday with 10 cases; and Thursday with 15 cases. In 5 cases the day of the week was not established.

### Social Vs Problem (Heavy) Drinking

It is noted that 50 percent of the cases tested were positive for alcohol. In a break down it is shown (again as in previous years) (1-10) that it is the problem (heavy) drinker who contributed to most of these fatalities.

	Approx. alcohol *
0.15 gm/dl and above-83 (62 <sup>0</sup> /o)	9 oz
0.10 - 0.14 - 21 (16 <sup>0</sup> /o)	6 oz
0.09 and less - 30 (22 <sup>0</sup> /o)	3 oz

78 percent of all traffic fatalities that were positive for alcohol were very high (above 0.10 gm/dl) this suggest drinking *at least* 6 oz of 80 proof.

62 percent were very very high (above 0.15 gm/dl) which suggests *more* than 9 oz of 80 proof.

These figures are similar to those obtained in previous years (1968-1975) (3-10).

It is the problem (heavy) drinker (who represents only 10 percent of the total drinking population in Puerto Rico) who is responsible for most of our traffic fatalities. *Somehow* we must try to "curb" this problem drinker who is so prone to killing himself and others.

### Age Group and Sex Distribution That Showed Most Positive Alcohol

36 males . . . . . Ages 21 to 30  
2 females . . . . . Ages 41 to 50

\*. Person 160 lb drinking 80 proof within 2 hours.

Sex Distribution of Driver and Pedestrian  
 Positive for Alcohol

Driver . . . 49 (48 males and 1 female)  
 Pedestrian . . 47 (45 males and 2 females)

TEENAGE (15-20) AND ALCOHOL INVOLVEMENT IN PREVIOUS YEARS  
 Compared with 1976

TEENAGERS  
 (15-20 yrs)

	1976	1975	1974
<i>Total Cases</i>	33(28M:5F)	47(38M:9F)	39(35M:4F)
<i>Positive Alcohol</i>	12(M)	15(13M:2F)	6(M)
<i>Driver</i>	10(9M:1F)	14(13M:1F)	14(M)
<i>Pedestrian</i>	9(8M:1F)	11(8M:3F)	8(7M:1F)
<i>Passenger</i>	10(7M:3F)	16(13M:3F)	11(9M:3F)
<i>Motorcyclist</i>	2(M)	3(2M:1F)	2(M)
<i>Bicyclist</i>	1(M)	3(M)	4(M)
<i>N. I. A. *</i>	1(M)	----	----
<i>Percent Alcohol</i>			
<i>0.09 percent or less</i>	4(M)(2Pa; 1Mo; 1Dr)	5(3Pa; 2Dr(1F)	1(M)(Pa)
<i>0.10-0.14 percent</i>	4(M)(2Dr; 1Pa; 1NIA)	5(4Dr; 1Pa)	5(2Pe; 1Pa; 1Dr; 1Mo)
<i>0.15 percent and over</i>	4(M)(3Dr; 1Pa)	5(4Pa(1F); 1Dr)	1(M)(Pa)

\* - N. I. A. - No information available.

TEENAGERS  
 (15-20 yrs)

	1973	1972	1971	1970
<i>Total Cases</i>	60(48M:12F)	43(34M:9F)	35(30M:5F)	32(30M:2F)
<i>Positive Alcohol</i>				
<i>0.09 or less</i>	9 (M)	9(8M:1F)	5 (M)	6 (M)
<i>0.10-0.14 gm/dl</i>	3 (M)	1 (M)	3 (M)	4 (M)
<i>0.15 and over</i>	2 (M)	5(4M:1F)	1 (M)	0

These above data (1970-1976) show that our teenagers are slowly becoming more involved in our traffic fatalities while drinking; This is SAD! And even more sad is the fact that more than a few of these cases, involved heavy drinking.

Percent comparison of previous years of driver and pedestrian positive for alcohol.

Year	Positive Alcohol	
	Pedestrian	Driver
1968	44 percent	78 percent
1969	45 percent	67 percent
1970	60 percent	63 percent
1971	56 percent	67 percent
1972	65 percent	70 percent
1973	42 percent	60 percent
1974	34 percent	48 percent
1975	43 percent	63 percent
1976	44 percent	61 percent

### Comment

How can anything that taste so good and is imbibed so freely — be so deadly? The answer is simple:

“BY DRINKING LIKE A FOOL:” — TOO MUCH, TOO SOON.

It is no longer “social drinking” when a person drinks more than 4 or 5 oz of rum or whiskey within a short interval. This is “Problem Drinking”.

### References

1. *Kaye, Sidney*: Blood alcohol levels and the driver. Bol. Asoc. Med. de P. R. 56: 115, 1964
2. *Kaye, Sidney, & Cardona, Eduardo L.*: Some question's in the evaluation of the blood alcohol levels in man. Proc. 4th. Int. Conf. on Alc. and Traff., Ind. Univ., Dec. 1965. Alcohol & Traffic Safety; Bloomington, Indiana Univ. Press 1966. pp: 178-181.
3. (a). *Kaye, Sidney*: Proceedings: Correlation between the blood level and fatal traffic accidents in Puerto Rico. Third Triennial Congress; International Assoc. for Accident &

- Traffic Medicine, 29 May, 1969, New York City: Proceedings, 28 May, 1969 - 5 June, 1969, also reported in:
- (b). *Kaye, Sidney*: Blood alcohol levels and fatal traffic accidents (1968). Bol. Asoc. Med. P. R. 61: 244, 1969.
4. *Kaye, Sidney*: Manslaughter on the highways (Puerto Rico 1969). Proceedings of 7th. Interamerican Conferences on Toxicology and Occupational Medicine, University of Miami, School of Medicine, Aug 17-20, 1970.
5. *Kaye, Sidney*: The “drunk” pedestrian and driver on our highways in Puerto Rico (1970). Bol. Asoc. Méd. P. R., 63: 170, 1971.
6. *Kaye, Sidney*: Influence of alcohol and drugs in traffic fatalities in Puerto Rico (1971). Fourth Congreso de Inter. Amer. do Prevencion de Riesgos Profesionales, San Juan, P. R., May 21-27, 1972.
7. *Kaye, Sidney*: Influence of alcohol on traffic deaths in Puerto Rico (1972). Bol. Asoc. Med. P. R., 65: 135, 1973.
8. *Kaye, Sidney*: Incidence of alcohol, drugs and carbon monoxide in traffic fatalities in Puerto Rico (1973). Proceedings of 6th. International Conference on Alcohol, Drugs and Traffic Safety, Toronto, Canada, Sept. 8-13, 1974.
9. *Kaye, Sidney*: Sudden drop in alcohol and drug related traffic fatalities in Puerto Rico (1974). Bol. Asoc. Med. de P. R., 67: 369, 1975.
10. *Kaye, Sidney*: The problem drinker and traffic fatalities in P. R. (1975). Proceedings of the Association of Clinical Scientists, Puerto Rico, April 22, 1975. Abstracted in An. Clin. & Lab. Sci., 6: 356, 1976.
11. *Kaye, Sidney*: Changing patterns of poisoning in Puerto Rico - Alcohol: The number one drug problem. Bol. Med. Asoc. P. R., 66: 64, 1974.
12. *Kaye, Sidney*: Alcohol and its effects on Man, Bol. Asoc. Med. P. R., 63: 302, 1971.
13. *Kaye, Sidney*: Toxicology of alcohol and the problems of drinking. Military Medicine, 141: 602, 1976.
14. *Kaye, Sidney*: (a). Proceedings of the Joint Annual Meeting of the College of American Pathologists and the American Society of Clinical Pathologists in Miami and reported in the Resident and Staff Physician, Feb. 1976:  
(b). Alcohol and traffic deaths, 22: 63, 1976.  
(c). When is a person drunk?, 22:67, 1976.
15. Personal communication with Dr. Carlos A. Aviles Roig, Assistant Secretary on Alcoholism and Addiction, Depto. de Servicio Contra la Adicción (July 10, 1975).
16. Dept. of Public Works and Transportation, Commonwealth of Puerto Rico.
17. Dept. of Police, Commonwealth of Puerto Rico.
18. *Kaye, Sidney*: The influence of alcohol on traffic fatalities, (a). Proceedings of the joint annual meeting of the American College of Pathologists and the American Society of Clinical Pathologists. Oct. 6-8, 1974, Washington, D. C., and republished.  
(b). Alcohol and traffic fatalities in booklet: “The professional and community role of the pathologist in alcohol abuse, Edited by George Lundberg, U. S. Dept. of Transportation, Natl. Hlway Traffic Safety Adm., HHS 802-161, Dec. 1976.



# TETANO: PATOFISIOLOGIA, CLINICA, TRATAMIENTO Y PREVENCIÓN

Héctor F. Gorbea, MD y Carlos H. Ramírez Ronda, MD, FACP

**Summary:** We present in a concise form the problem of tetanus in Puerto Rico, a serious public health problem that remains with us in spite of the massive immunization campaign efforts. The pathophysiology, clinical presentation and management of tetanus are summarized. Our emphasis is on prevention since we are able to prevent tetanus 100 percent all of the time. We believe that the programs of community education have been effective, since tetanus in the neonate and young adult is almost non-existent. We must be cautious and not overconfident; a single tetanus toxoid injection is not protective, three injections are required. We are sure that tetanus toxoid and tetanus immune globulin are overused in our emergency rooms. We strongly endorse the recommendations of the Advisory Committee on Immunization practices on the management of the patient with wounds. In spite of all the joint efforts of physicians, and private agencies, tetanus is with us. We see tetanus today in our senior citizens, the adult 60 years of age and older. Our senior citizens have a false sense of security, they feel protected against tetanus because they received a tetanus shot sometime in the past; their

immunity is nil and they are the victims of tetanus after a minor wound, skin ulcer or just poor oral hygiene. We want to make the medical community aware of the problem in this age group so that we might direct our efforts to immunize our patients, specially those 60 years of age and older. Once our entire population is immunized, tetanus will be a minor problem.

**Resumen:** Presentamos en una forma breve el problema del tétano en Puerto Rico, un problema de salud pública que persiste entre nosotros a pesar de los esfuerzos de inmunización masiva. La patofisiología y el cuadro clínico se describen. Queremos enfatizar la prevención, ya que el tétano es una enfermedad que podemos prevenir un 100 por ciento de las veces. Creemos que los programas de educación a la comunidad y las campañas de inmunización han surtido efecto. La incidencia del tétano en el neonato y el adulto joven es muy baja. Debemos de tener cautela y no sentirnos sobreconfiados; una inyección de toxoide aislada no es protectora, se requieren tres inyecciones. Estamos seguros que en nuestras salas de emergencia sobreusamos el toxoide y endosamos las recomendaciones del Comité Asesor Sobre Prácticas de Inmunización para el manejo del paciente con heridas. A pesar de los esfuerzos unidos de los médicos, las agencias gubernamentales y privadas, el tétano está con nosotros. Lo vemos hoy en el adulto entrado en años, usualmente 60 años o más, el cual como consecuencia de un falso sentido de seguridad, ya que posiblemente en el pasado recibió una inyección de toxoide, no mantiene

---

*De la Sección de Enfermedades Infecciosas, Departamentos de Investigación y Medicina, Hospital de Veteranos y la Escuela de Medicina de la Universidad de Puerto Rico, San Juan, Puerto Rico.*

*Favor de solicitar reimpresos a: Carlos H. Ramírez Ronda, MD, Jefe, Laboratorio de Investigación de Enfermedades Infecciosas (151), Hospital de la Administración de Veteranos, GPO Box 4867, San Juan, Puerto Rico 00936.*

su inmunidad al día y es víctima del tétano después de recibir una herida menor, tener una úlcera en la piel o una higiene oral pobre. Queremos que la comunidad médica esté consciente de este problema y que dirijamos nuestros esfuerzos a inmunizar los pacientes mayores de 60 años. Una vez inmunizemos toda nuestra población, el tétano pasará a ser un problema menor.

### Introducción

El tétano ha sido un problema serio de salud pública en Puerto Rico (1) con una incidencia 16 veces mayor que la de los Estados Unidos de América (2, 3, 4). En 1965-66 el Departamento de Salud inició un programa de inmunización masiva para el control de la enfermedad. Esto resultó en una baja en la incidencia del tétano en niños; más a pesar de este programa, la morbilidad del tétano no se redujo en los neonatos ni en los adultos mayores de 40 años (5). A pesar de los esfuerzos de inmunización en masa utilizando el toxoide de tétano, un método de prevención que es simple, efectivo y con muy pocas reacciones adversas serias, el tétano todavía está con nosotros y muchos puertorriqueños sucumben. En los últimos seis años, 1970-1975, se han reportado 96 casos de tétano en Puerto Rico al Departamento de Salud. En 1975 se reportaron 19 casos en Puerto Rico para una incidencia de 0.66 casos por 100,000 habitantes. En contraste, en EE.UU. la incidencia de tétano reportado al Centro de Control de Enfermedades en Atlanta en 1975 fue de 0.04 casos por 100,000 habitantes. Si tomamos en consideración que la mortalidad a causa del tétano es de alrededor de 60 por ciento y que la incidencia en Puerto Rico es 16 veces la de Estados Unidos, entonces es fácil notar que esta enfermedad es un problema serio de salud pública de nuestro pueblo. El agente causante de esta enfermedad es el *Clostridium tetani*, un organismo aneróbico que forma esporas. Las esporas pueden ganar acceso al

cuerpo a través de una herida contaminada y si la herida resulta en tejido necrótico, el potencial local de oxidación se reduce creando el ambiente propicio para que la espora germine, convirtiéndose en la forma vegetativa y produciendo toxinas las cuales son responsables del cuadro clínico del tétano. *Clostridium tetani*, en su forma vegetativa, es positivo para la tinción de Gram y es mótil. En su forma de espora tiene una apariencia característica de raqueta de tenis, con las esporas al final. La germinación de esporas ocurre tanto en tejidos como *en vitro*. Las formas vegetativas son susceptibles al calor y a varios desinfectantes, mientras que las esporas son altamente resistentes. Estas pueden sobrevivir en la tierra, si no son expuestas a la luz solar por meses y años.

El portal de entrada del tétano es usualmente una herida, mayormente en las extremidades, pero también puede ser una úlcera de piel crónica, otitis media crónica, abscesos dentales e incisiones quirúrgicas. La enfermedad mayormente afecta personas en actividades al aire libre siendo grupos de alto riesgo los agricultores, jardineros, personal militar, deportistas y personas en trabajos manuales. El tétano hoy en día es menos común en niños debido a la práctica efectiva de la inmunización activa de rutina en infantes, sin embargo en los últimos años la incidencia del tétano ha aumentado en los envejecientes. Estudios hechos en nuestro laboratorio confirman que un número significativo de adultos mayores de 60 años no tienen niveles de protección (anticuerpos circulantes) en contra del tétano, reflejando un estado de protección pobre en este grupo de nuestra población (6).

Todas las manifestaciones clínicas del tétano son producidas por la actividad de la exotoxina, una neurotoxina llamada tetanoespasmina. También la bacteria produce una hemolisina. La tetanoespasmina interfiere con la transmisión neuromuscular inhibiendo la descarga de acetilcolina de los terminales nerviosos

en los músculos. En el cordón espinal causa una disfunción de los reflejos polisinápticos que envuelven las neuromas intermedias produciendo una inhibición de antagonistas, o sea, inhibe el mecanismo de inhibición de estímulos. Esta acción es responsable del fenómeno primordial del tétano, la hipertoncicidad del músculo esquelético con espasmos (7, 8).

### Presentación Clínica

El período de incubación del tétano en humanos es usualmente de dos a 56 días de duración, aunque se podría extender hasta varios meses en algunos casos. Mientras más corto sea el período de incubación más alta será la mortalidad y peor el pronóstico (9).

Hay tres formas clínicas del tétano: local, generalizado y cefálico (9). La manifestación que caracteriza el tétano local es una rigidez persistente de los músculos próximos al lugar del daño tisular. Los síntomas pueden persistir por varias semanas y hasta por meses en algunos casos, finalmente desapareciendo sin dejar residuos. Esta forma clínica del tétano es leve, la mortalidad es de alrededor de 1 por ciento. El tétano local puede preceder el desarrollo de una forma generalizada que es la forma más común del tétano. La segunda forma, el tétano generalizado, en el 80 por ciento de los casos la contaminación ocurre a través de una herida menor. El tétano generalizado puede presentarse como una rigidez del cuello, de los músculos abdominales, dificultad al tragar, irritabilidad, nerviosismo y malestar general. Más de la mitad de los casos presentan como síntomas, espasmos de los músculos de masticación. También son comunes las contracciones de los músculos de la quijada, cara, cuello, espalda y abdomen. El espasmo de los músculos de masticación produce una expresión facial que caracteriza el tétano, la risa sardónica. La contracción intensa y persistente de los músculos de la espalda producen opistótono. Una convulsión típica del tétano se caracteriza por una contracción súbita de grupos de músculos, causando flexión

y abducción de los brazos, cerrando los puños encima del tórax y extensión de las extremidades inferiores. Durante estos episodios el paciente no pierde el conocimiento pero sí siente dolores de gran intensidad. El paciente puede presentar también disfagia, sudoración, fiebre y espasmo de la laringe o glotis. Estas últimas manifestaciones pueden causar cianosis y asfixia si no se atiende a tiempo (10). La tercera forma clínica, el tétano cefálico, tiene un pronóstico pobre. Esta forma ocurre con muy poca frecuencia, teniendo un período de incubación de uno a dos días. Casi siempre es precedida por heridas en la cabeza o por otitis media. La característica es la disfunción de los nervios craneales, siendo el séptimo par craneal el que se afecta con más frecuencia. En algunos casos, la forma cefálica puede preceder la forma generalizada.

### Diagnóstico

El diagnóstico del tétano se hace principalmente a base de la presentación clínica y el historial pues los estudios de laboratorio ayudan muy poco. Examen del líquido cefalorraquídeo no demuestra anormalidades. El conteo de células blancas puede ser normal o elevado. Tinciones de Gram puede que no demuestren el organismo y cultivos anaeróbicos de material obtenido de las heridas son positivos en solo un 32 por ciento de los casos.

### Prognóstico

En general, la mortalidad a causa del tétano es de alrededor de 60 por ciento pero hay dos tipos de tétano generalizado que tienen un pronóstico poco favorable con una mortalidad alta: tétano en recién nacidos y en adictos a heroína (9, 11, 12).

### Tratamiento

El tratamiento del tétano envuelve varias



metas: 1) administrar antitoxina específica para neutralizar la toxina circulante antes de que llegue al sistema nervioso central; 2) excisión quirúrgica del lugar donde el organismo está produciendo la toxina; 3) cuidado intenso y constante velando por el balance de líquidos, electrolitos y calorías; 4) poner al paciente en un lugar tranquilo donde no haya ninguna clase de estímulos; 5) traqueostomía, si las convulsiones se convierten en problema.

Como cualquier estímulo puede causar espasmo o contracciones generalizadas, es necesario reducir todos los estímulos externos a un mínimo absoluto sedando el paciente y limitando las manipulaciones. El paciente se debe internar en un cuarto oscuro sin ruidos.

La antitoxina que se recomienda para el tratamiento del tétano es la globulina humana en una dosis de 3,000 a 6,000 unidades intramuscular. Cuando el tejido afectado no se puede remover, el uso de antitoxina localmente es de valor. En estos casos, la infiltración de 1,500 a 3,000 unidades puede llevarse a cabo (13).

La penicilina destruye las formas vegetativas de *Clostridium tetani*. En todos los casos de tétano se recomienda la administración intramuscular de 1.2 millones de unidades de penicilina procainada una vez al día, o un millón de unidades de penicilina G endovenosa cada cuatro horas por diez días. También se puede usar tetraciclina en dosis de dos gramos por día (13). Recomendamos la forma endovenosa para disminuir estimulación.

Para controlar las convulsiones y los espasmos se utilizan varios agentes: clorpromazina (Thorazine ®) es efectivo para controlar convulsiones y junto con barbitúricos es aún más efectivo (14). La dosis que se requiere para potenciar los hipnóticos es de 4 a 12 mg en infantes y de 50 a 150 mg en adultos cada cuatro a ocho horas. Secobarbital (Seconal ®) y pentobarbital (Nembutal ®) son muy útiles para sedar el paciente. El nivel óptimo de sedación es aquel en el cual el paciente descansa tranquilamente sin convulsiones, casi dormido,

pero que responda a estímulo. La dosis inicial es de 3 a 5 mg por kg de peso intramuscular para niños y de 100 a 150 mg intramuscular para adultos. Los requisitos diarios de estos agentes no se pueden predecir pues dependerán de la frecuencia y severidad de las convulsiones (15). Diazepam (Valium ®) se ha usado con éxito para prevenir y controlar las convulsiones del tétano. La dosis endovenosa es de 2 a 20 mg cada 2 a 8 horas; la cantidad e intervalo entre inyecciones depende de la severidad de la enfermedad (15, 16). En algunos casos se requiere anestesiarse al paciente (17).

Es muy importante recordar que los pacientes que recobran del tétano se deben inmunizar activamente pues la enfermedad no produce inmunidad natural (13).

### Prevención

La prevención constituye la base de la protección de la población en contra del tétano. El método que se usa es la inmunización activa con toxoide.

La inmunización primaria en niños consiste en una inyección de los toxoides de tétano y difteria más pertusis (DTP) a los 2 meses de edad seguido por una segunda inyección (0.5 ml) 2 meses después; una tercera inyección dos meses después de la segunda inyección y un refuerzo al año de la tercera dosis. El niño debe de recibir un refuerzo al llegar a la edad escolar (5 años de edad). Subsiguiente a esto el nivel de protección se mantiene con una dosis de refuerzo con la vacuna tipo adulto (Td) cada diez años. Véase Tabla I.

Un gran número de adultos en nuestra población no tiene un historial de inmunización claro. Para tener niveles de protección adecuados se requiere haber tenido una inmunización básica que consiste de una inyección inicial de 0.5 ml de toxoide de tétano, seguida por una segunda dosis de 4 a 6 semanas después de la primera y una tercera de 6 a 12 meses después de la segunda. Véase Tabla II. Una vez el pacien-

**TABLA I**  
**Inmunización Primaria Rutinaria de Niños en contra de Tétano,**  
**Difteria y Tos Ferina**

<i>Edad</i>	<i>Dosis</i>
<i>2 meses</i>	<i>DPT Núm. 1</i>
<i>4 meses</i>	<i>DPT Núm. 2</i>
<i>6 meses</i>	<i>DPT Núm. 3</i>
<i>18 meses</i>	<i>DPT refuerzo</i>
<i>5 años</i>	<i>DPT refuerzo</i>
<i>Cada 10 años</i>	<i>Td</i>

*DPT - Difteria, Tos ferina y Tétano (Toxoide)*

*Td - Tétano y difteria tipo adulto (Toxoide)*

**TABLA II**  
**Inmunización Básica**  
**Para Obtener Protección Adecuada Contra el Tétano**

<i>Primera Dosis-</i>	<i>0.5 ml toxoide de tétano</i>
<i>Segunda Dosis:</i>	<i>0.5 ml toxoide de tétano 4 a 6 semanas después de la primera dosis</i>
<i>Tercera Dosis:</i>	<i>0.5 ml toxoide de tétano 6 a 12 meses después de la segunda dosis</i>

te ha tenido esta experiencia de vacunación, se mantienen niveles protectivos adecuados con una dosis de refuerzo cada 10 años, bajo condiciones normales (18, 19, 20).

El problema mayor que se le presenta al médico es el manejo del paciente que llega a su oficina o a una Sala de Emergencia con una herida. Muchas veces todo paciente herido, irrespectivo del tipo de herida o su historial de inmunización, recibe una dosis de refuerzo del toxoide de tétano. Esta práctica se sobreutiliza

y puede ser perjudicial (18, 19). Nos encontramos que no solo se utiliza la inmunización activa con toxoide, sino que también se sobreutiliza la globulina humana antitetánica (Hypertet<sup>®</sup>). El Comité Asesor de Prácticas de Inmunización de los Estados Unidos de América ha hecho recomendaciones específicas para la prevención del tétano en pacientes con heridas (21, 22). Véase Tabla III.

Es imprescindible obtener el historial de inmunización del paciente herido, específica-

**TABLA III**  
**Recomendaciones del Comité Asesor**  
**en Prácticas de Inmunización de los Estados Unidos**  
**para la Prevención del Tétano en Pacientes con Heridas**

<i>Historial de Inmunización contra el Tétano</i>	<i>Heridas Limpias, Menores</i>		<i>Heridas Mayores</i>	
	<i>Toxoide</i>	<i>Globulina Humana</i>	<i>Toxoide</i>	<i>Globulina Humana</i>
<i>Desconocido</i>	<i>Sí</i>	<i>No</i>	<i>Sí</i>	<i>Sí<sub>4</sub></i>
<i>0-1</i>	<i>Sí</i>	<i>No</i>	<i>Sí</i>	<i>Sí<sub>4</sub></i>
<i>2</i>	<i>Sí</i>	<i>No</i>	<i>Sí</i>	<i>No<sub>2</sub></i>
<i>3 o más</i>	<i>No<sub>1</sub></i>	<i>No</i>	<i>No<sub>3</sub></i>	<i>No<sub>1</sub></i>

<sub>1</sub> *A menos que hayan pasado más de 10 años desde la última dosis*

<sub>2</sub> *A menos que tenga más de 24 horas*

<sub>3</sub> *A menos que hayan pasado más de 5 años desde la última dosis*

<sub>4</sub> *250 unidades*

mente el número de inyecciones de toxoide que ha recibido y la fecha de su última inyección. Es necesario conocer el tiempo que ha pasado desde que el paciente sufrió la herida, específicamente si es mayor o menor de 24 horas de duración. También es importante determinar si la herida es menor o es una herida mayor. Cuando el historial de inmunización es incierto o desconocido en un paciente con una herida menor y/o limpia, este debe recibir una inyección de toxoide solamente y hacer arreglos para completar una inmunización primaria. Un paciente con heridas mayores y con un historial de inmunización incierto debe recibir el toxoide y 250 unidades de globulina humana antitetánica. El mismo manejo se utiliza si el paciente tiene un historial de inmunización de una sola inyección de toxoide. El paciente con historial de haber recibido 2 inyecciones de toxoide con una herida menor se maneja en forma similar a lo arriba descrito, más cuando tiene una herida mayor de 24 horas o más de duración, debe recibir además la inmunización pasiva con globulina humana antitetánica. El

paciente con un historial de inmunización completo, 3 inyecciones o más de toxoide, con una herida menor, no debe recibir toxoide a menos que hayan pasado 10 años desde la última inyección. Cuando este paciente tiene una herida mayor debe recibir una inyección de toxoide sin han pasado 5 años desde la última y debe recibir la globulina humana antitetánica si han transcurrido 10 años.

El esfuerzo mayor de prevención debe estar dirigido a nuestra población de personas de 60 años o más, las cuales en su mayoría no están protegidas y exhortamos a la clase médica a inmunizar estos pacientes siguiendo las recomendaciones expuestas anteriormente.

### Referencias

1. Rivera, J. V.: El tétano: un reto. Editorial. Bol. Asoc. Med. PR 54: 91-93, 1962.
2. Rodríguez, H. F., García Moliner, L., Visot Fernández, L.: Tetanus: An analysis of 546 cases. Bol Asoc Med PR 57: 377-384, 1965.



3. Ratner, L. H., Steeves, R., Ramírez-Smith, K., Mainardi, L.: Retrospective analysis of tetanus in Puerto Rico. *Bol. Asoc. Med. PR* 62: 22-29, 1970.
4. Rodríguez, H. F.: Tetanus: Report of 268 cases. *Bol. Asoc. Med. PR* 5: 362-368, 1959.
5. Larrieu, A. J., García-Moliner, L., Rodríguez, H. F.: Tetanus in Southern Puerto Rico after a mass vaccination program. *Bol. Asoc. Med. PR* 65: 131-134, 1973.
6. Gorbea, H. F., LLuberes, R., Ramírez-Ronda, C. H.: Tetanus antitoxin levels in Puerto Rican males: A preliminary report. *Bol. Asoc. Med. PR* 68: 319, 1976 (Abstract).
7. Parsons, R. L., Hoffman, W. W., Feigen, G. A.: Mode of action of tetanus toxin on the neuromuscular junction. *Amer. J. Phys.* 210: 84-90, 1966.
8. Brooks, V. B., Curtis, D. R., Eccles, J. C.: Mode of action of tetanus toxin. *Nature (Lond)* 175: 120-121, 1955.
9. La Force, F. M., Young, L. S., Bennet, J. V.: Tetanus in the United States (1965-1966): epidemiologic and clinical features. *N. Engl. J. Med.* 280: 569-574, 1969.
10. Kerr, J. H., Corbett, J. L., Prys-Roberts, C. et al: Involvement of the sympathetic nervous system in tetanus: Studies on 82 cases. *Lancet* 2: 236-241, 1968.
11. Levinson, A., Marske, R. L., Shein, M. K.: Tetanus in heroin addicts. *JAMA* 157: 658-660, 1955.
12. Cherubin, C. E.: Clinical severity of tetanus in narcotic addicts in New York City. *Arch. Intern. Med.* 121: 156-158, 1968.
13. Young, L. S., LaForce, F. M., Bennet, J. V.: An evaluation of serological and antimicrobial therapy in the treatment of tetanus in the United States. *J. Infect. Dis.* 120: 153-159, 1969.
14. Cole, A. C. E., Robertson, D. H. H.: Chlorpromazine in the management of tetanus. *Lancet* 2: 1063-1064, 1955.
15. Perlstein, M. A., Stein, M. D., Elam, H.: Routine treatment of tetanus. *JAMA* 173: 1536-1541, 1960.
16. Cordova, A. B.: Control of the spasm of tetanus with diazepam (Valium): evaluation of clinical usefulness based upon observation of three childhood cases. *Clin. Pediatr.* 8: 712-716, 1969.
17. Jenkins, M. T., Luhn, N. R.: Active management of tetanus: based on experiences of an anesthesiology department. *Anesthesiology* 23: 690-709, 1962.
18. Peebles, T. C., Levine, L., Eldried, M. C. et al: Tetanus-toxoid emergency boosters: A reappraisal. *N. Engl. J. Med.* 280: 575-581, 1969.
19. Edsall, G., Elliot, M. W., Peebles, T. C. et al: Excessive use of tetanus toxoid boosters. *JAMA* 202: 111-113, 1967.
20. Pratt, E. L.: Clinical tetanus: a study of fifty-six cases, with special references to methods of prevention and a plan for evaluating treatment. *JAMA* 129: 1243-1247, 1945.
21. Fraser, D. W.: Preventing tetanus in patients with wounds. Editorial. *Ann. Int. Med.* 84: 95-97, 1976.
22. Smith, J. W. G., Lawrence, D. R., Evans, D. G.: Prevention of tetanus in the wounded. *Brit. Med. J.* 2: 453-455, 1975.

TEMPORAL ARTERITIS

Víctor M. Mojica, MD, Alejandro Franco, MD and Radamés Sierra, MD

Temporal arteritis, although infrequent, must be considered in the differential diagnosis of headache in the elderly. This entity, if not diagnosed and treated properly, may lead to serious complications and death.

Giant cell arteritis is a better term than temporal arteritis for this disease of unknown etiology, since this process is a generalized vascular disease of the large and medium-sized arteries. Although any of the intracranial vessels can be affected, especially involved are the ophthalmic and retinal vessels, causing transient visual disturbances in 50 percent of the cases and blindness in 25 percent of these patients. Involvement of the carotids may produce transient ischemic attacks and inflammation of the coronaries may result in myocardial infarction.

Considering the almost invariably favorable response to corticosteroid therapy, the early recognition of this disease is absolutely essential in order to avoid these tragic complications. The purpose of this presentation is to alert the physician to the recognition of this syndrome.

Four cases from my personal experience and two from the Rheumatology Institute were detected in the years 1973-74. A search through five major hospitals in the San Juan Metropolitan area was made reviewing the records covering approximately a 10-year period. Only one

more case was found for a total of seven.

The clinical manifestations of the cases to be described are summarized and are similar to those reported in the literature available. The ages of the patients varied between 60 and 85 years; four were females and two were males. Headaches, either generalized or localized with general malaise, were the main complaints in all but one of the patients that presented polymyalgias with a previous history of pain in the temporal region and jaw. Jaw pain, myalgias in the cervical shoulder girdle, polymyalgias, weight loss, fever, anorexia, vertigo, dysphagia and facial spasms were among the other symptoms found. Focal signs like tenderness in the temporal region were found in the majority (5 out of 7) and a prominent or an indurated temporal artery in three patients.

The sedimentation rate by the Wintrobe method was elevated in all of the patients ranging from 36 mm/hr to 121 mm/hr. In two patients the alpha-2 globulin fraction was elevated and the hemoglobin was below normal in four. Biopsy of the temporal artery showed histological evidence of arteritis in all except one case, but the response to Prednisone was favorable in all of them. The initial total daily dose of Prednisone was 30 mg in one, 40 mg in three, and 60 mg in three. One patient, who received 30 mg for a three-month period, had a flare-up of symptoms when the drug was discontinued, requiring reinstitution of treatment. Another patient, after ten months of treatment with 7.5 mg of Prednisone daily, developed polymyalgias requiring higher doses for effective control of symptoms. Alternate-day corticosteroid regimen was tried in two patients without success. This is the same expe-

---

*From the Neurology Section, Medical Service, Veterans Administration Center, G. P. O. Box 4867, San Juan, Puerto Rico 00936.*

*Address reprint requests to Víctor M. Mójica, MD.*

rience found at the Mayo Clinic where this type of treatment modality was tried unsuccessfully.

Giant cell arteritis may be present with vague non-specific systemic complaints from a period of five months to two years before the diagnosis is established. Among the clinical spectrum of this disease, Polymyalgia Rheumatica is important and is characterized by pain and stiffness in the proximal muscles; neck and shoulders or pelvic girdle; along with systemic manifestations such as fever, malaise, weight loss, depression and anorexia. This form may then turn into temporal arteritis. On the other hand, temporal arteritis may lead to polymyalgia or both may occur simultaneously.

In most cases, the temporal artery biopsy shows inflammatory cells within the vessel wall, more pronounced in the medial layer, with predominance of mononuclear cells, lymphocytes, histiocytes, and giant cells. However, this may be absent in an inadequate biopsy specimen due to the segmental distribution of the arteritic process. Thrombosis, at the site of active inflammation is also a frequent finding. The biopsy is generally risk free and, if multiple sections of the biopsied material are examined, the yield of positive findings is higher.

The sedimentation rate is almost invariably elevated but in approximately 10-15 percent it may be persistently normal.

It should be stressed that the dose of Prednisone recommended is between 40-80 mg daily for a duration of eight months to two years.

If the treatment is of short duration and the dose is below the above, the relapse rate is close to 30 percent.

Finally, I must stress that although the incidence of this condition in Puerto Rico appears to be low, the clinician must consider temporal or giant cell arteritis in elderly people who complain of polymyalgia or headaches with other non-specific systemic manifestations.

A registry of this condition is being maintained at the San Juan VA Hospital and all cases that fulfill the diagnostic criteria are welcome.

### References

1. Fauchald, P., et al: Temporal arteritis and polymyalgia rheumatica. *Ann Int Med* 77: 845, 1972.
2. Bragatani: Anarthritic rheumatoid disease. *Lancet* 2: 694-697, 1965.
3. Cooke, et al: Temporal arteritis: A generalized vascular disease. *Qtr. J Med* 15: 47-75, 1946.
4. Harrison, M. J. C. and Bevan, A. T.: Early symptoms of temporal arteritis. *Lancet* 2: 638-640, Sept. 23, 1967.
5. Hunder, G. and Allen, G. L.: *Geriatrics*. 28 (6), June, 1973.
6. Dixon, A. J., Beardwell, C., and Kay, A., et al: Polymyalgia rheumatica and temporal arteritis. *Ann Rheu Dis* 25: 203-288, 1966.
7. Hunder, G., et al: Daily and alternate-day corticosteroid regimens in treatment of giant cell arteritis. *Ann Int Med* 82 (5): 613-618, May, 1975.
8. Dickson, E. R.: Systemic giant cell arteritis with polymyalgia rheumatica. *JAMA* 224: 1496-1498, 1973.
9. Allen-Hauser, W., Ferguson, R. H., et al: Temporal arteritis in Rochester, Minnesota. *Mayo Clin Proc.* 46: 597-602, Sept., 1971.





## Natural balance doesn't always come naturally

Big Balanced Rock, Chiricahua Mountains, Arizona (approx 1,000 tons)

- **Most Widely Prescribed**—Antivert is the most widely prescribed agent for the management of vertigo\* associated with diseases affecting the vestibular system such as Menière's disease, labyrinthitis, and vestibular neuronitis.
- **Relief of Nausea and Vomiting**—Antivert/25 can relieve the nausea and vomiting often associated with vertigo\*.
- **Dosage for Vertigo\***—The usual adult dosage for Antivert/25 is one tablet t.i.d.

#### BRIEF SUMMARY OF PRESCRIBING INFORMATION

\*INDICATIONS. Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows:

**Effective:** Management of nausea and vomiting and dizziness associated with motion sickness.

**Possibly Effective:** Management of vertigo associated with diseases affecting the vestibular system.

Final classification of the less than effective indications requires further investigation.

**CONTRAINDICATIONS.** Administration of Antivert (meclizine HCl) during pregnancy or to women who may become pregnant is contraindicated in view of the teratogenic effect of the drug in rats.

The administration of meclizine to pregnant rats during the 12-15 day of gestation has produced cleft palate in the offspring. Limited studies using doses of over 100 mg./kg./day in rabbits and 10 mg./kg./day in pigs and monkeys did not show cleft palate. Congeners of meclizine have caused cleft palate in species other than the rat.

Meclizine HCl is contraindicated in individuals who have shown a previous hypersensitivity to it.

**WARNINGS.** Since drowsiness may, on occasion, occur with use of this drug, patients should be warned of this possibility and cautioned against driving a car or operating dangerous machinery.


**Usage in Children:** Clinical studies establishing safety and effectiveness in children have not been done; therefore, usage is not recommended in the pediatric age group.

**Usage in Pregnancy:** See "Contraindications."

**ADVERSE REACTIONS.** Drowsiness, dry mouth and, on rare occasions, blurred vision have been reported.

More detailed professional information available on request.

**ROERIG**   
A division of Pfizer Pharmaceuticals  
New York, New York 10017

**Antivert<sup>®</sup>/25**   
(meclizine HCl) 25 mg. Tablets  
**for vertigo\***

# TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE **DYAZIDE<sup>®</sup>**

Each capsule contains 50 mg. of Dyrenium<sup>®</sup> (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### \* Warning

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

\* **Indications:** When the combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium sparing action of triamterene is warranted. (See Box Warning.) Routine use of diuretics in healthy pregnant women is inappropriate; they are indicated in pregnancy only when edema is due to pathological causes.

**Contraindications:** Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K<sup>+</sup> levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K<sup>+</sup> intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids).

Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum K<sup>+</sup> frequently; both can cause K<sup>+</sup> retention and elevated serum K<sup>+</sup>. Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis.

'Dyazide' interferes with fluorescent measurement of quinidine.

### Adverse Reactions:

Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions;

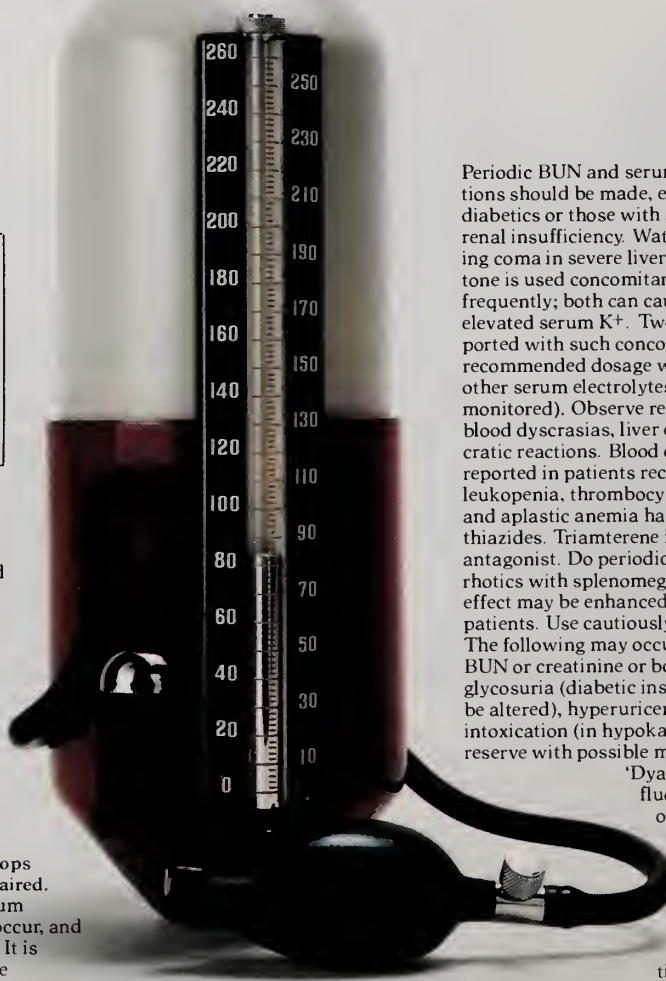
nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).

**FOR LONG-TERM CONTROL  
OF HYPERTENSION\*  
SERUM K<sup>+</sup> AND BUN SHOULD  
BE CHECKED PERIODICALLY.  
(SEE WARNINGS SECTION.)**

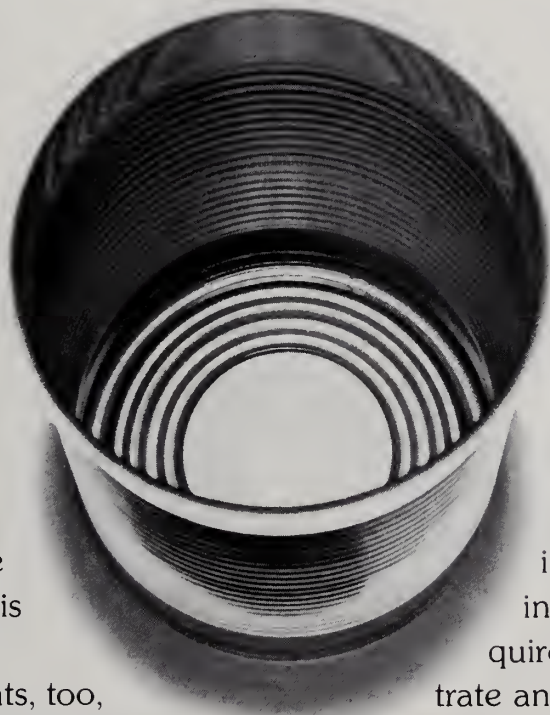
SK&F CO., Carolina, P.R. 00630

**SK&F CO.**  
a SmithKline company





# NOW a two-piece 14oz. can for Soyalac



A two-piece can means no soldered seam. No solder means no possibility of lead contamination from the container. Soyalac is the first infant formula with this packaging innovation.

There are improvements, too, in the formulation. Soyalac now has 25% more iron than known competitive hypoallergenic milk-free formulae. In fact, the entire formula has been slightly modi-

fied to reflect the current U.S. RDA levels set by the Food and Drug Administration.

Soyalac—formula for infants on regular feeding and for those who require milk-free diets; concentrate and single strength, ready-to-use. Made from the whole soybean. I-Soyalac concentrate, made from soy isolate, with no soy carbohydrates and **no corn products**.



For detailed information and samples call or write:

Western U.S.  
LOMA LINDA FOODS  
11503 Pierce Street  
Riverside, CA 92515  
(714) 785-2444

Eastern U.S.  
LOMA LINDA FOODS  
13246 Wooster Road  
Mount Vernon, OH 43050  
(614) 397-7077

**Loma Linda**®



# B.W.CO. HAS PUT MORE POTENCY IN THE LINE



**EMPRACET® with Codeine Phosphate, 60 mg, No. 4** Ⓢ

**EMPRACET® with Codeine Phosphate, 30 mg, No. 3** Ⓢ

**CONTRAINDICATIONS:** Hypersensitivity to acetaminophen or codeine.

**WARNINGS: Drug dependence.** Codeine can produce drug dependence of the morphine type and may be abused. Dependence and tolerance may develop upon repeated administration; prescribe and administer with same caution appropriate to oral narcotics. Subject to the Federal Controlled Substances Act.

**Usage in ambulatory patients.** Caution patients that these products may impair mental and/or physical abilities required for performance of potentially hazardous tasks such as driving a car or operating machinery.

**Interaction with other CNS depressants.** Patients receiving other narcotic analgesics, general anesthetics, phenothiazines, tranquilizers, sedative-hypnotics, or other CNS depressants (including alcohol) may exhibit additive CNS depression; when used together reduce dose of one or both.

**Usage in Pregnancy.** Safe use is not established. Should not be used in pregnant patients unless potential benefits outweigh possible hazards.

**PRECAUTIONS: Head injury and increased intracranial pressure.** Respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a pre-existing increase in intracranial pressure. Narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries.

**Acute abdominal condition.** These products or other narcotics may obscure the diagnosis or clinical course of acute abdominal conditions.

**Special risk patients.** Administer with caution to certain patients such as elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, or prostatic hypertrophy or urethral stricture.

**ADVERSE REACTIONS:** Most frequently include lightheadedness, dizziness, sedation, nausea, and vomiting; more prominent in ambulatory than in nonambulatory patients; some may be alleviated if patient lies down; others include: euphoria, dysphoria, constipation and pruritus.

**DRUG INTERACTIONS:** CNS depressant effect may be additive with that of other CNS depressants. See Warnings.

For symptoms and treatment of overdosage and full prescribing information, see package insert.

## Introducing **EMPRACET®** **̄ CODEINE #4**

Each tablet contains: codeine phosphate,  
60 mg (1 gr) (Warning—may be habit-forming);  
and acetaminophen, 300 mg.



### Our new non-aspirin/ codeine analgesic for moderate to severe pain.

New peach-colored Empracet ̄ Codeine #4 offers a potent alternative for patients in whom aspirin is not indicated.

Unlike compounds containing oxycodone which afford comparable analgesia, new Empracet ̄ Codeine #4 gives you CIII prescribing convenience—up to 5 refills in 6 months at your discretion (where state law permits). And, prescribing by telephone is permissible in most states. Moreover, new Empracet ̄ Codeine #4 has less addiction potential than does oxycodone.

For those of your patients requiring a less potent analgesic, non-aspirin Empracet® ̄ Codeine #3 provides effective relief of moderate pain.

**Burroughs Wellcome Co. makes codeine combination products. You make the choice.**



**Burroughs Wellcome Co.**  
Research Triangle Park  
North Carolina 27709

## DENGUE

---

En agosto de 1977 la actividad del dengue aumentó en nuestra isla con la época de lluvia. Por consiguiente, hubo un incremento en el número de casos y posiblemente un brote epidémico en la región Norte de Puerto Rico. El dengue es endémico en Puerto Rico y se han documentado epidemias en los años 1963, 1969 y 1975 (1, 2, 3). Cada brote ha sido estudiado, y una vez se controla el vector *Aedes aegyptii* o el número de personas susceptibles disminuye, el brote termina.

El dengue es una enfermedad causada por un arbovirus y hay cuatro serogrupos distintos de los virus de dengue. El serogrupo más común en Puerto Rico es el número 2. El virus de dengue se transmite de mosquito a humano y desconocemos que exista un reservorio no humano para el virus. El mosquito *Aedes aegyptii* llega a proporciones críticas durante la época de lluvia, ya que tiene la oportunidad para reproducirse en pequeños estancamientos de agua y en lugares donde se acumula basura húmeda.

Cuando ocurren brotes de dengue, el número de personas afectadas clínicamente es de 24 por cada cien, con una tasa de infección serológica de hasta un 73 por ciento. Debemos de saber que por cada persona con un cuadro clínico de dengue, posiblemente existan 2 con infección subclínica (4). El dengue clásico se caracteriza por un cuadro prodrómico de conjuntivitis y/o coriza, seguido por un dolor de cabeza que comienza súbitamente 5 a 8 días después de la picada del mosquito. Hay dolor retroorbital, dolor de espalda, dolores articulares y musculares. El dolor de cabeza se agrava con el movimiento y hay dolor al mover los ojos. Se puede encontrar linfadenopatía y frecuentemente se ve una erupción evanescente en el tronco, que en algunas personas puede ser prurítico y terminar por descamación. En la mayoría de los casos la fiebre persiste de 5 a 6 días y termina súbitamente. En otros casos, la fiebre desaparece en dos días para recurrir. Este síndrome clásico de fiebre, malestar, linfadenopatía y erupción es benigno.

En Puerto Rico se ha venido estudiando el dengue desde los años 60 y buscando sus complicaciones. En el área del Pacífico del Sur y el Sureste de Asia el cuadro de dengue se caracteriza por fiebre hemorrágica, usualmente en niños, y difiere del cuadro clásico de dengue en que los dolores musculares, articulares y óseos son poco comunes (5). Este síndrome se caracteriza por petequias, sangrías y muerte en un número significativo de casos. En estos casos encontramos hemoconcentración, contejes leucocitarios normales, trombocitopenia, prueba de torniquete positiva, hiponatremia, acidosis e hipoproteinemia (6). A pesar de que en las epidemias de la Costa del Golfo de Estados Unidos en 1922 se describieron manifestaciones hemorrágicas, no fue hasta 1968 que se describió un caso en el Caribe (Curazao) (8). No hubieron muertes en esta ocasión. En el año 1972 se describió un caso en Puerto Rico de una persona con el cuadro clínico de dengue que presentó trombocitopenia, hipoproteinemia, hemoconcentración, acidosis y shock. Esta persona murió (9).

Durante la epidemia de 1975 empezamos a notar la asociación de casos de dengue con manifestaciones hemorrágicas. Es el cuadro de dengue clásico con trombocitopenia, prueba de torniquete positiva y manifestaciones hemorrágicas. Estas manifestaciones fueron transitorias y no se atribuyó muerte alguna.



El dengue está nuevamente con nosotros; estamos observando un número significativo de pacientes con trombocitopenia y niveles de plaquetas tan bajo como 11,000. ¿A qué se debe este fenómeno? La pregunta no tiene una respuesta clara. En el Sureste de Asia el síndrome se asocia a una segunda infección con un virus de dengue heterólogo (10). Una vez ocurre una respuesta anamnésica de IgG, se activan las cascadas de complemento y éstas son responsables por el cuadro clínico. La severidad del dengue se ha correlacionado con el nivel de C3. En Puerto Rico usualmente no tenemos experiencia con varios tipos de dengue, por lo tanto, la trombocitopenia que observamos no puede explicarse necesariamente por una respuesta inmunológica. Se ha descrito en Tahití (11) dengue hemorrágico con una infección primaria y puede ser que esto es lo que estamos observando.

En Puerto Rico tenemos dengue y estamos observando trombocitopenia con médulas óseas que revelan arresto en la maduración de megakariocitos y otros cambios en estas células. Sabemos que los salicilatos, tales como la aspirina, interfieren con la función plaquetaria (12). Basándonos en los pacientes observados, sugerimos que al paciente en el cual se sospeche dengue, no se le administre aspirina o productos con aspirina; puede utilizar acetaminofen si usted lo desea. Es importante que a este paciente se le haga un hemograma completo incluyendo conteo de plaquetas. También se debe hacer una prueba de torniquete. Si el conteo de plaquetas está significativamente bajo ( $\leq 50,000$ ) el paciente debe hospitalizarse. Se debe considerar un examen de médula ósea. Notifique el caso al Centro de Control de Enfermedades, 781-3636. Siga los parámetros de hematocrito, proteínas totales, plaquetas y signos vitales. Evite la deshidratación, previniendo la sobrehidratación. La mayoría de los pacientes recobrarán en 4 a 5 días con terapia conservadora. Si el conteo de plaquetas está bajo (30,000), el uso de corticoesteroides, prednisona 60 mg/día puede considerarse. De usar corticoesteroides, debe ser por corto tiempo y debe discontinuarse lo más rápido posible una vez las plaquetas estén normales.

Carlos H. Ramírez Ronda, MD, FACP

## Referencias

1. Neff, J. M., Movis, L., González-Alcover, R., Coleman, P. H., Lyss, S. B. and Negran, A.: Dengue fever in a Puerto Rican community. *Amer J Epidemiol* 86: 162-184, 1967.
2. Likosky, W. H., Calisher, C. H., Michelson, A. L., Correa-Coronas, R., Henderson, B. E. and Feldman, R. A.: An epidemiologic study of dengue type 2 in Puerto Rico, 1969. *Amer J Epidemiol* 97: 264-275, 1973.
3. Morales, H., Madera, J. E., Ramírez-Ronda, C. H., Bermúdez, R. H., González, V. and Rommey, H.: Follow-up on dengue-Puerto Rico. *Morb and Mort Week Rep* 25: 7, 1976.
4. Sanford, J. P.: Dengue fever. In: *Principles of Internal Medicine*. Thorn, G. W., Adams, R. A., Brunwald, E., Isselbacher, K. J. and Petersdorf, R. G. (eds.), 8th Ed. McGraw Hill Book Co., 1977, pp. 1048-1049.
5. Halstead, S. B., Udomsakdi, S., Singharaj, P. and Nisalak, A.: Dengue and chikunya virus infection in man in Thailand, 1962-1964. III. Clinical, epidemiological and virological observations on disease in non-indigenous white persons. *Amer J Trop Med Hyg* 18: 984-996, 1969.
6. Pongpanich, B. and Kumonpant, S.: Studies on dengue hemorrhagic fever. V. Hemodynamic studies of clinical shock associated with dengue hemorrhagic fever. *Tropical Pediatrics* 83: 1073-1077, 1973.
7. Ehrenkranz, N. J., Ventura, A. K., Cuadrado, R. R., Pond, W. L. and Porter, J. E.: Pandemic dengue in Caribbean countries and the Southern United States. Past - present and potential problems. *New Engl J Med* 285: 1460-1469, 1971.
8. Sar, A. van der: An outbreak of dengue hemorrhagic fever in Curacao. *Trop Geogr Med* 25: 119-129, 1973.
9. Ramírez-Ronda, C. H., Maldonado, N., Rabell, V., Cline, B. L. and Sather, G.: Dengue hemorrhagic shock syndrome in Western Hemisphere: A case report. (Submitted for publication).
10. Memoranda: Pathogenic mechanisms in dengue hemorrhagic fever. Report of an international collaborative study. *Bull WHO* 48: 117-133, 1973.
11. Barnes, W. J. S. and Rosen, L.: Fatal hemorrhagic disease and shock associated with primary dengue infection on a pacific island. *Amer J Trop Med Hyg* 23: 495-506, 1974.
12. Caprino, L.: Anti-inflammatory drugs and platelet aggregation. In: *Platelet Aggregation and Drugs*. Caprino, L. and Rossi, E. C. (eds) Academic Press, 1974, pp. 143-150.



*AMA NEWS RELEASE:*

*HERBAL HEALTH PILLS CAUSE LEAD POISONING*

CHICAGO — Yet another case of accidental lead poisoning from health food products is reported in the Oct. 3 Journal of the American Medical Association.

A California housewife was poisoned by herbal health pills imported from Hong Kong. Earlier this year the Journal reported the case of a Hollywood actress poisoned by a powdered bone meal health food product imported from England.

The 59-year-old woman had consulted a herbalist-acupuncturist for pains in her joints, say Drs. Johnson Lightfoote, H. Joseph Blair and James R. Cohen of Stanford University School of Medicine.

The practitioner instructed her to take two types of herbal pills, one orange and one red, three times daily. She took the pills regularly for several months, along with acupuncture treatments, but developed pains in shoulder, neck, back, knee, hip, breasts and abdomen, as well as insomnia, irritability and paranoia. Her pills were analyzed and found to contain a high amount of lead. The pills were stopped and therapy started to get the lead out of her system, and improvement was rapid.

"The herbalist-acupuncturist was interviewed by us as well as by the Food and Drug Administration and the Public Health Service. Efforts are underway to find other possible patients at risk. The herbalist had obtained the pills from Hong Kong and was not aware of their lead content," says the Journal report.

In an accompanying editorial, William H. Crosby, MD, of the Scripps Clinic and Research Foundation, La Jolla, Calif., points out that the FDA does not at present have the resources to do a proper job of surveillance of the health food industry. No official standards have been established, says Dr. Crosby, of acceptable levels of lead in foods.

The FDA has been picking up and analyzing samples of powdered bone meal from health food stores across the country in the wake of the case of the poisoned actress, he says.

*NEW ASTHMA DRUGS AID SUFFERERS*

CHICAGO — Asthma sufferers in the United States are finally benefitting this fall from two important new drugs that have been available in Britain for many years.

Two separate reports in the Oct. 3 Journal of the American Medical Association evaluate the two drugs and report that they are useful in control of asthma.

D. Robert Webb, MD, of the Mason Clinic, Seattle, reports on administering one of the drugs, beclomethasone dipropionate, to 30 patients with chronic bronchial asthma whose condition was so severe that it required corticosteroid therapy with prednisone. After three months most of those receiving the new drug were able to discontinue prednisone. After six months, adrenal function improved and steroid toxic reactions decreased. The drug, given as an aerosol, was generally well-tolerated and effective, says Dr. Webb.

Beclomethasone dipropionate has been available in Great Britain since 1973, but only recently was released for use in the U. S., he says.

The other new product, cromolyn sodium, has been marketed throughout the world since 1968, but only recently has become available in the U. S. It is evaluated by Michael H. Dykes, MD, senior scientist with the AMA's Department of Drugs, in the Oct. 3 JAMA.

Cromolyn sodium is a unique and effective anti-asthmatic agent, Dr. Dykes concludes, and its continuous use will benefit a large proportion of asthmatic patients. In many it will be most effective when administered with other standard drugs.

---

*AMA DELEGATES TO MEET DEC. 4-7*

CHICAGO — The 1977 interim session of the House of Delegates of the American Medical Association will be held Dec. 4-7 in Chicago (Palmer House).

Official notification of the meeting is published in the Oct. 3 Journal of the American Medical Association.

Sessions will begin at 2 p.m. Sunday, Dec. 4, and continue through Wednesday, Dec. 7.

For the first time the AMA's Winter Scientific Meeting, formerly known as the Clinical Convention, will be held separately from the House of Delegates.

The Scientific Meeting will be held Dec. 10-13 in Miami Beach, Fla. It will feature continuing education courses for physicians.

---

#### *SURGERY WITHOUT TRANSFUSIONS IS PROVED SAFE*

CHICAGO — Cardiovascular operations can be performed safely without blood transfusions, says a report by Texas M.D.s David A. Ott and Denton A. Cooley in the Sept. 19 Journal of the American Medical Association.

Drs. Ott and Cooley, of the Texas Heart Institute, Houston, report on a 20-year experience of surgery performed on 542 Jehovah's Witness patients, who refuse blood transfusions for religious reasons. Early mortality rate was 9.4 percent.

Only three of the 51 deaths were related directly to loss of blood. Postoperative anemia was a contributing factor in 12 other deaths. The other deaths were from causes not related to loss of blood.

"Our experience supports the contention that patients who refuse blood transfusion for religious reasons can undergo major cardiovascular operations with an acceptably low risk," say Drs. Ott and Cooley.

Discussing their experience in performing heart and blood vessel surgery on members of the fundamentalist religious body, the Texas doctors declare:

"The surgeon who agrees to treat Jehovah's Witnesses should respect their religious beliefs or refer them elsewhere. To our knowledge, no claims have been made against a physician for failing to administer blood to a Jehovah's Witness.

"We believe that a patient should have a right to make his or her own decision, and that the physician

has a moral responsibility to respect the wishes of the patient. We have never violated the contract made before operation that blood will not be administered regardless of the circumstances or need."

In the case of children, if extensive blood loss is anticipated surgery should not be recommended, they say.

---

#### *FEW GAIN WORK CAPACITY AFTER HEART ARTERY SURGERY*

CHICAGO — Coronary artery bypass surgery relieves the severe chest pains of heart disease in thousands of individuals each year, but the procedure contributes little to getting these individuals back to work, says a report in the Sept. 19 Journal of the American Medical Association.

Glenda K. Barnes, RN, and colleagues at the Medical Center of the University of Birmingham (Ala.) analyzed the work capacity of 350 patients who had coronary artery bypass grafting procedures, to determine change in work status as a result of the operation.

"Overall, there was no improvement in return to work or hours worked after surgery," says Ms. Barnes.

An estimated 65,000 coronary bypass procedures are being performed annually in the United States at an approximate cost of at least \$10,000 each, Ms. Barnes points out. Justification for these complex and costly procedures is based primarily on relief of pain and improvement of the "quality of life," rather than the increased survival demonstrated in a few subgroups, she says.

At least 70 to 80 percent of such patients get partial or complete relief of their angina in the early years after operations. Such data would suggest that the majority of these patients can be expected to return to work and more productive lives after surgery.

But this doesn't happen.

"In the group of 350 patients studied before and one year after coronary bypass grafting, there was no noticeable increase of work activities postoperatively. Forty-four percent of the patients decreased their hours worked per week, 24 percent remained the same, and 32 percent increased hours worked. Thus,

there was no net improvement in status."

Physical or mental demands of the job may have precluded some of the persons from working, Ms. Barnes says. Fear of such stress causing further heart problems may be a deterrent. Others may not return to work because of lack of incentive, especially money. Some may draw more from disability apyments than they could earn on the job. Others cannot return to work because of company or union policies concerning heart patients.

"Clearly, more emphasis must be placed on the rehabilitation of postcoronary bypass patients if return to work is a desireable goal of these costly procedures."

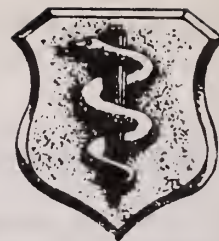
*EL I CURSO INTERNACIONAL DE TRASPLANTE RENAL* tendrá lugar en Barcelona, España, los días 24, 25 y 26 de abril de 1978. Este curso está organizado por la Cátedra de Urología, la Unidad de Trasplante Renal y el Servicio de Inmunología del Hospital Clínico y Provincial.

Siendo sus directores el Prof. J. Ma. Gil-Vernet y los Dres. A. Caralps y J. Vives. En el se discutirán temas de interés para urólogos, nefrólogos e inmunólogos y se harán operaciones de trasplante renal que serán transmitidas por televisión; los cursillistas que lo deseen podrán hacer prácticas sobre técnicas inmunológicas.

Para más información, escribir al Dr. J. Masramón, Cátedra de Urología, C/ Casanova, 143, Barcelona, España.



# United States Air Force



USAF MEDICAL RECRUITING OFFICE  
CASO BUILDING, STOP 18  
1225 PONCE DE LEON  
SANTURCE, PUERTO RICO 00907  
722-5014 or 753-4398

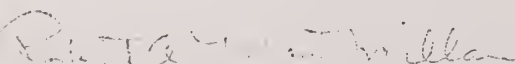
## PHYSICIANS

Since termination of the Draft in 1973, the Air Force has experienced tremendous success in recruiting volunteer physicians from civilian life for service in our medical facilities. A major factor for this success is the Variable Incentive Pay bonus that raised the minimum starting salary for physicians to approximately \$33,000.00 per year. This starting salary can be significantly higher depending on training, experience, and military service (active or reserve). Guaranteed assignment--prior to commitment--to one of our 135 medical facilities located throughout the free world has also attracted many physicians to the Air Force. Other inducements include opportunity for travel, 30 days paid vacation per year, generally shorter working hours than experienced in civilian practice, opportunity to practice medicine without the ominous specter of soaring malpractice insurance rates, excellent medical facilities with total ancillary and administrative support, and many other fringe benefits.

Basic criteria are US citizenship or permanent alien registration (I-151); maximum 56 yrs old; one year postgraduate AMA-approved medical education; permanent, unrestricted state medical license, and be able to pass an Air Force commissioning physical.

A personal conference with you would enable me to determine what rank and pay scale the Air Force can offer you. Please telephone me at the above numbers so we can discuss our program in greater detail and schedule a mutually acceptable appointment.

Sincerely

  
ROBERT A. MACMILLAN, MSGT USAF  
Health Professions Recruiter

HEALTH PROFESSIONS RECRUITING

# New tablet size announcement

## Septra<sup>®</sup>

Each tablet contains:  
80 mg trimethoprim and  
400 mg sulfamethoxazole

OLD SIZE:



NEW SIZE:



## Septra<sup>®</sup> DS

Each tablet contains:  
160 mg trimethoprim and  
800 mg sulfamethoxazole

OLD SIZE:



NEW SIZE:



# B.W. Co.<sup>®</sup> has made Septra and Septra DS easier to swallow



Wellcome

Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

**anti-  
inflammatory**

**antifungal**

**antipruritic**

**antibacterial**





# Clear choice

When dermatoses become infected with bacteria or fungi, plain topical steroids are generally not the recommended therapeutic choice.

A clear choice, however, is Vioform<sup>®</sup>-Hydrocortisone. With its unique four-way action, it supplies the kind of comprehensive treatment many common dermatoses\* require.

\*This drug has been evaluated as possibly effective for these indications. See brief prescribing information.

## Vioform<sup>®</sup>-Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis; impetiginized eczema; nummular eczema; infantile eczema; endogenous chronic infectious dermatitis; stasis dermatitis; pyoderma; nuchal eczema and chronic eczematoid otitis externa; acne urticata; localized or disseminated neurodermatitis; lichen simplex chronicus; anogenital pruritus (vulvae, scroti, ani); folliculitis; bacterial dermatoses; mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis); moniliasis; intertrigo. Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds; lesions of the eye; tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, and varicella).

### WARNINGS

*This product is not for ophthalmic use.*

In the presence of systemic infections, appropriate systemic antibiotics should be used.

### Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant females has not been established. Therefore, they should not be used extensively on pregnant patients in large amounts or for prolonged periods of time.

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If this occurs, discontinue therapy. May stain.

If used under occlusive dressings or for a prolonged period, watch for signs of pituitary-adrenal axis suppression.

May interfere with thyroid function tests. Wait at least one month after discontinuance of therapy before performing these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine.

Prolonged use may result in overgrowth of nonsusceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

Few reports include: Hypersensitivity, local burning, irritation, pruritus. Discontinue if untoward reaction occurs. Rarely, topical corticosteroids may cause striae at site of application when used for long periods in intertriginous areas.

### DOSAGE

Apply a thin layer to affected areas 3 or 4 times daily.

### HOW SUPPLIED

**Cream**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 5 and 20 Gm. **Ointment**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base; tubes of 20 Gm.

**Lotion**, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water; plastic squeeze bottles of 15 ml. **Mild Cream**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water; tubes of 1/2 and 1 ounce.

**Mild Ointment**, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base; tubes of 1 ounce.

C75-38 Rev. 7/75

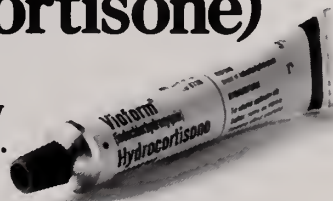
Consult complete product literature before prescribing.

CIBA Pharmaceutical Company  
Division of CIBA-GEIGY Corporation  
Summit, New Jersey 07901

2/7853 17

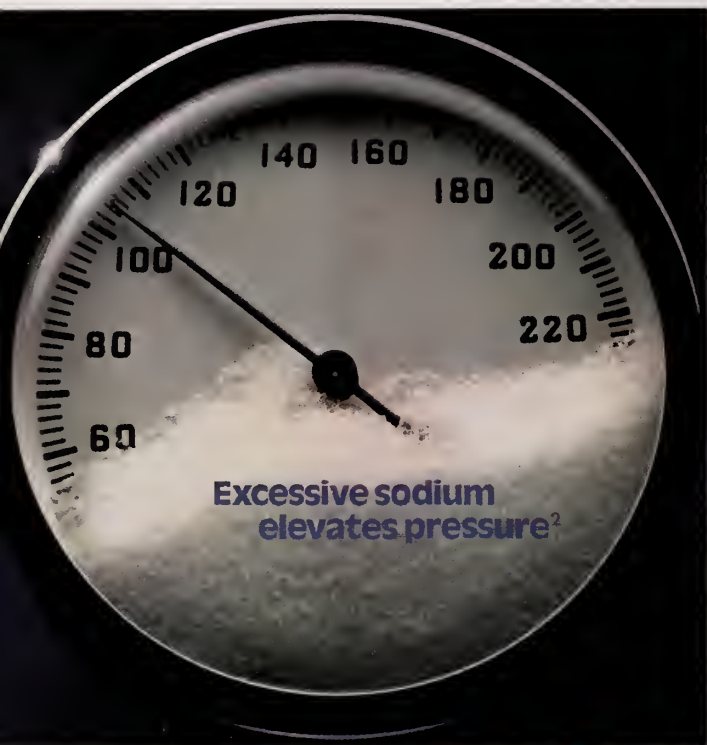
# Vioform<sup>®</sup>- Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

The most widely  
prescribed form...  
20-Gm Cream



C I B A

# In hypertension...



## Hygroton® 50 mg. (chlorthalidone USP)

### As step-1 therapy

Sustained control of sodium retention is important for sustained control of hypertension. Hygroton blocks sodium retention longer than any other diuretic available.

### As baseline diuretic in step-2 therapy

Reserpine, methyldopa and propranolol may cause compensatory sodium retention. For this reason, the National Task Force<sup>1</sup> recommends diuretics as the baseline in step-2 therapy. Hygroton is an "ideal" choice because of its sustained blockade of sodium retention.

# Hygroton® 50 mg. (chlorthalidone USP) one a day Blocks sodium retention longer

#### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema.

**Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance; namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug

may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance.

**Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn.

**Usual Dose:** One tablet daily.

**How Supplied:** Tablets—100 mg (white, scored) and 50 mg (aqua) in bottles of 100 and 1000; PAKs of 28 tablets, boxes of 6.

#### References:

1. Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure: A Cooperative Study, JAMA 237:255, January 17, 1977.
2. Laragh, J.H. et al.: Vasoconstriction—volume analysis for understanding and treating hypertension: The use of renin and aldosterone profiles, in Hypertension Manual (Laragh, J.H., ed.), New York, Dun-Donnelley, 1974, pp. 824-825.

**USV  
LABORATORIES**

USV Laboratories Inc.  
Manati, P.R. 00701



Unlock arthritis pain  
and inflammation with  
the right combination!

# Ascriptin® A/D

Arthritic Doses



## Aspirin 325 mg.

*Still* the rheumatologist's  
anti-inflammatory analgesic drug  
of choice for the control of arthritis.

## Maalox® 300 mg.

*Still* the gastroenterologist's antacid  
of choice, providing dependable gastric  
protection at optimum dosage levels.

## Ascriptin® A/D

Now a better approach for salicylate control  
of arthritis with less gastric irritation  
(as illustrated by endoscopy\*).

\*Data on file, William H. Rorer Medical Department.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034



## LISTA DE ANUNCIANTES

1. BOEHRINGER INGELHEIM  
Torecan
2. BURROUGHS WELLCOME  
Codeine Anal., Septra
3. CIBA PHARM.  
Vioform - HC
4. EATON LAB.  
Macrochantin
5. LOMA LINDA FOOD  
Soyalac
6. ROCHE LAB.  
Bactrim, Librium, Valium
7. ROERIG & CO.  
Antivert
8. W. H. RORER  
Ascriptin
9. SMITH, KLINE & FRENCH  
Dyazide
10. U.S.V. PHARM.  
Hygroton

## Macrochantin® (nitrofurantoin macrocrystals)

Capsules 25 mg 50 mg 100 mg

**INDICATIONS:** Indicated for the treatment of pyelonephritis, pyelitis, and cystitis due to susceptible *E. coli*, enterococci, *S. aureus* (it is not indicated for the treatment of associated renal cortical or perinephric abscesses) and certain strains of *Klebsiella-Aerobacter*, *Proteus* and *Pseudomonas*.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function; infants under one month; pregnant patients or term; known hypersensitivity.

**WARNINGS:** May cause hemolytic anemia of the primaquine sensitivity type, apparently linked to a glucose-6-phosphate dehydrogenase deficiency. (Such patients should be closely observed while receiving nitrofurantoin.) Discontinue the drug at any sign of hemolysis. Hemolysis ceases on withdrawal. Superinfections (limited to the genitourinary tract) may occur, most commonly due to *Pseudomonas*. Safety not established during pregnancy and lactation; should not be used in women of childbearing potential unless the expected benefits outweigh the possible hazards.

**PRECAUTIONS:** Peripheral neuropathy may occur. A fatality has been reported. Predisposing conditions such as renal impairment, anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**ADVERSE REACTIONS: Gastrointestinal Reactions—**Anorexia, nausea, emesis are the most frequent reactions; less frequently, abdominal pain and diarrhea; rarely, hepatitis. This dose-related toxicity reaction can be minimized by reduction of dosage, especially in the female patient.

**Hypersensitivity Reactions—**Pulmonary sensitivity reactions, which can be acute, subacute, or chronic. Acute reaction is commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on X-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and resolve with cessation of the drug therapy. Subacute or chronic pulmonary reaction is associated with prolonged therapy. Insidious onset of malaise, dyspnea on exertion, cough, altered pulmonary function, and roentgenographic and histologic findings of diffuse interstitial pneumonitis of fibrosis or both are common manifestations. Impaired pulmonary function may result even after cessation of the drug therapy.

**Dermatologic Reactions—**Muculopopular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other Sensitivity Reactions—**Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and orthostatic hypotension.

**Hematologic Reactions—**Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurological Reactions—**Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

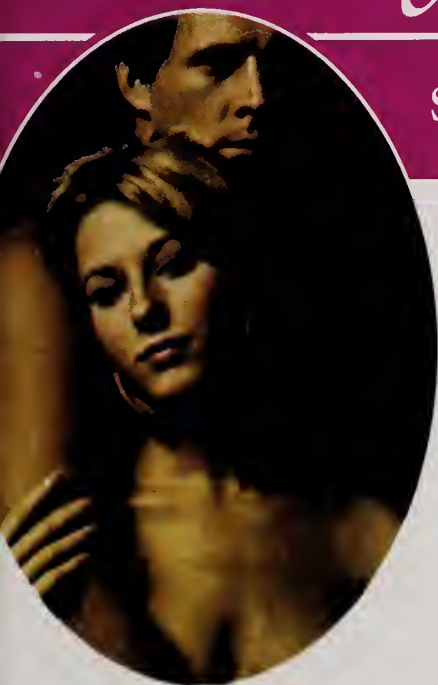
**Miscellaneous Reactions—**Transient alopecia.

**SUPPLIED:** Macrochantin (nitrofurantoin macrocrystals) is available in opaque, yellow capsules of 100 mg (coded "Eaton 009") and in opaque, yellow and white capsules of 50 mg (coded "Eaton 008") in bottles of 30, 100, 500, and 1,000 capsules; and in opaque, white capsules of 25 mg (coded "Eaton 007") in bottles of 100 capsules. Macrochantin Capsules, 50 mg and 100 mg, are also available in hospital unit-dose packages, strip-packaged in boxes of 100.



**EATON LABORATORIES**  
Norwich International  
Division of Morton-Norwich Products, Inc.  
410 Park Avenue, New York, N.Y. 10022, U.S.A.

# Recurrent UTI\* in the Sexually Active Female



## Special Problems of Management

### A. General measures

- Showering rather than tub-bathing
- Showering before intercourse
- Voiding after intercourse

### B. Antimicrobial therapy

■ Overt episodes of urinary tract infection\* should be treated with a standard course of Macrochantin® therapy, until there is evidence of bacteriologic cure.

However, for the women who have recurrent UTI associated with sexual intercourse, *long-term suppressive therapy* is recommended, including...

■ **Nightly antibacterial therapy:** An oral dose at bedtime for several months or longer (one 50 mg or one 100 mg Macrochantin® capsule) for the patient who has a continuing "chronic" cystitis. The rationale for the bedtime dose is that during this period the bladder remains unemptied for the longest interval.



Capsules  
25 mg 50 mg 100 mg

## Macrochantin® (nitrofurantoin macrocrystals)

**Consistent potency against the  
most prevalent uropathogens**

\*Macrochantin® is effective in cystitis, pyelitis and pyelonephritis due to susceptible organisms.  
See brief summary on facing page.

## To relieve nausea and vomiting associated with

- postoperative recovery
- radiation therapy
- chemotherapy
- acute situations

(Contraindicated in pregnancy, severe CNS depression, comatose states and in patients who have demonstrated a hypersensitivity to phenothiazines.)

## Three dosage forms with the same 10 mg dosage strength:

**Tablets**—10 mg (thiethylperazine maleate, NF)



**Suppositories**—10 mg (thiethylperazine maleate, NF)



**Injection**—10 mg/2cc ampul (thiethylperazine maleate, NF) for IM use only.



# Torecan<sup>®</sup>

(thiethylperazine)

Still available in  
Puerto Rico



**Boehringer Ingelheim**

Boehringer Ingelheim Ltd.  
Elmsford, New York 10523

**Torecan<sup>®</sup>** (thiethylperazine)

Tablets, Suppositories and Injection

**Contraindications:** Severe CNS depression, comatose states, and in patients who have demonstrated a hypersensitivity to phenothiazines (e.g., blood dyscrasias, jaundice). Because severe hypotension has been reported after the intravenous administration of phenothiazines, this route of administration is contraindicated. The drug is contraindicated in pregnancy.

**Warnings:** Phenothiazines are capable of potentiating CNS depressants as well as atropine and phosphorous insecticides. The drug may impair mental and/or physical ability required in the performance of potentially hazardous tasks such as driving a car or operating machinery.

**Postoperative Nausea and Vomiting:** When used to control postoperative nausea and vomiting in patients undergoing elective surgical procedures, restlessness and postoperative CNS depression during anesthesia recovery may occur. Possible postoperative complications of a severe degree of any of the known reactions of this class of drug must be considered. Postural hypotension may occur after an initial injection, rarely with the tablet or suppository. Do not use with epinephrine in the treatment of drug-induced hypotension as phenothiazines may induce a reversed epinephrine effect. The most suitable vasoconstrictor agents are levaterenol and phenylephrine. The use of Torecan has not been studied following intracardiac and intracranial surgery. Not recommended for use in children under 12 years of age, or in nursing mothers since safety and efficacy have not been established.

**Precautions:** Convulsions and abnormal movements such as extrapyramidal symptoms have occurred. The varied extrapyramidal symptom complex is more likely to occur in young adults and children. Extrapyramidal effects must be treated by reduction of dosage or cessation of medication. For treatment of nausea and/or vomiting associated with anesthesia and surgery, the drug should be administered by deep intramuscular injection at or shortly before the termination of anesthesia.

**Adverse Reactions:** CNS: convulsions, extrapyramidal symptoms such as dystonia, torticollis, oculogyric crisis, akathisia and gait disturbances, occasional cases of dizziness, headache, fever and restlessness have been reported. Drowsiness may occur initially on injection but is usually alleviated by a reduction in dosage. Dryness of the mouth and nose, blurred vision, tinnitus, sialorrhea and altered gustatory sensation. Peripheral edema of the arms, hands and face. Cholestatic jaundice, cerebral vascular spasm and trigeminal neuralgia have been reported occasionally. The following have occurred with phenothiazine derivatives and should be considered: agranulocytosis, leukopenia, thrombocytopenia, aplastic anemia, pancytopenia, eosinophilia, leukocytosis, miosis, obstipation, anorexia, paralytic ileus, erythema, exfoliative dermatitis and contact dermatitis; jaundice, biliary stasis. Hypotension, rarely leading to cardiac arrest, ECG changes. Akathisia, agitation, motor restlessness, dystonic reactions, trismus, torticollis, opisthotonos, oculogyric crises, tremor, muscular rigidity, akinesia, some of which have persisted for several months or years especially in patients of advanced age with brain damage. Menstrual irregularities, altered libido, gynecostasia, weight gain; false positive pregnancy tests. Urinary retention, incontinence; fever, laryngeal edema and angioneurotic edema, asthma. Hyperpyrexia, behavioral effects suggestive of a paradoxical reaction, including excitement, bizarre dreams, aggravation of psychoses and toxic confusional states. ECG changes. While there is no evidence that ECG changes are in any way precursors of any significant disturbance of cardiac rhythm, sudden and unexpected deaths apparently due to cardiac arrest have been reported in a few instances in hospitalized psychotic patients previously showing characteristic ECG changes. A peculiar skin-eye syndrome, which is marked by progressive pigmentation of areas of the skin or conjunctiva and/or accompanied by discoloration of the exposed sclera and cornea, has also been recognized as a side effect following long-term treatment. Opacities of the anterior lens and cornea described as irregular or stellate in shape have also been reported.

**Drug Interactions:** Phenothiazines are capable of potentiating CNS depressants (e.g., anesthetics, opiates, alcohol, etc.) as well as atropine and phosphorous insecticides. The drug may induce a reversed epinephrine effect on occasion.

For complete details, please see full prescribing information.





# ASOCIACION MEDICA DE PUERTO RICO

DISPLAY  
SHELVES

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
BOSTON

BOLETIN

THE FRANCIS A. COUNTWAY  
LIBRARY OF MEDICINE  
10 SHATTUCK STREET  
BOSTON, MASS. 02115



VOL. 69

Diciembre 1977

No. 12

# A character all its own.

Valium (diazepam) is a benzodiazepine with a character all its own.

Pharmacologically, it has been described as more potent mg-per-mg than other available anxiolytic benzodiazepines. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> (diazepam)<sup>IV</sup>

2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



— A NUESTROS PATROCINADORES —

*En este año a punto de terminar, la Junta Editora desea expresar su agradecimiento a nuestros patrocinadores del Boletín de la Asociación Médica de Puerto Rico, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos. Son éstos proveer un medio para la publicación de artículos científicos de nuestros médicos, informar a nuestros lectores de problemas médicos de importancia, proporcionar vías de comunicación para expresar puntos de vista; tanto oficiales como de índole personal, estimular liderato médico para la solución de nuestros problemas; en fin, lograr una revista de actualidad que refleje la calidad de la medicina Puertorriqueña.*

*Agradecemos la ayuda y apoyo de nuestros patrocinadores.*

— TO OUR ADVERTISERS —

*In this year about to end, the Editorial Board recognizes with gratitude the aid provided by those advertising in the Boletín de la Asociación Médica de Puerto Rico, whose support permits the fulfillment of our objectives. These are to provide the medium for publication of scientific articles by our physicians, to keep our readers informed of diverse medical problems of importance, to provide communication means for the expression of different points of view, to stimulate medical leadership for the solution of our problems, in short, to produce a journal which will reflect the quality of Puerto Rican medicine.*

*We sincerely thank our advertisers for their help and continued support.*

LISTA DE ANUNCIANTES

- |                          |  |
|--------------------------|--|
| 1. BURROUGHS WELLCOME    | NEOSPORIN, SEPTRA                      |
| 2. PHARM. MFG.           | INSTITUTIONAL                          |
| 3. ROCHE LAB.            | AZO GANTANOL, BACTRIM, LIBRIUM, VALIUM |
| 4. RORER INTERNATIONAL   | MAALOX                                 |
| 5. SMITH, KLINE & FRENCH | DYAZIDE                                |



Organó Oficial

Fundado en 1903

Volumen 69

Diciembre 1977

Número 12

## JUNTA EDITORA

Jose L. Cangiano, Presidente; Herman J. Flax; Norman I. Maldonado; F. Hernández Morales; Francisco Olazábal, Jr.; Nathan Rifkinson; Enrique O. Velez García; Antonio J. Grillo; Mario R. García Palmieri; Rafael Villavicencio Jiménez; E. A. Santiago Delpín; Ramón H. Bermúdez; Manuel Martínez Maldonado; José Juan Corcino; Jesus M. Vázquez; Osvaldo Ramírez Muxó.

## SECRETARIO DE REDACCION

Sr. Gregorio Díaz

### Oficina Administrativa:

Edificio de la Asociación Médica de Puerto Rico, Ave. Fernández Juncos Núm. 1305, Apartado de Correos 9387, Santurce, Puerto Rico 00908. Tel. 725-6969.

### Anuncios, Suscripciones y Reimpresos:

El Boletín se publica mensualmente. El precio de suscripción es de \$10.00 al año. Todo material de anuncio está sujeto a aprobación por la Junta Editora. La tarifa de precios para anuncios será suministrada a solicitud. Copia del anuncio debe ser recibida el día primero del mes que precede al mes de publicación. Representante de anuncios nacionales es la State Medical Journal Advt. Bureau, 711 South Blvd., Oak Park, Illinois 60302.

Podrán ordenarse reimpresos de los artículos a publicarse cuando se reciba notificación de su aceptación.

### Trabajos Científicos:

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica. El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista. La AMPR no se hace responsable de las opiniones y declaraciones vertidas por los autores y sus puntos de vista no necesariamente representan aquellos de la AMPR; cualquier relación con la política oficial es coincidencia.

## CONTENIDO

Neuroblastoma: Eight Year Experience. ....	386
<i>Pedro J. Rosselló, MD, Pedro J. Santiago Borrero, MD and Víctor A. Marcial, MD</i>	
Changing Patterns in Poisoning in Puerto Rico 1972-1976. ....	396
<i>Sidney Kaye, MSc, PhD</i>	
Editorial: Nefrología 1977. ....	398
<i>Osvaldo Ramírez Muxó, MD</i>	
Discurso Toma de Posesión como Presidente de la Asociación Médica de Puerto Rico. ....	398
<i>Rafael Berríos Martínez, MD</i>	
Nota Biográfica Dr. Rafael Berríos Martínez. ....	401
Noticias. ....	402
Reconocimiento a Arbitros. ....	405
Contenido. ....	408
Indice de Autores. ....	415
Indice de Materias. ....	418

## NUESTRA PORTADA

*Convento de los Dominicos-Viejo San Juan*

*Cortesía del Banco Gubernamental de Fomento*

# NEUROBLASTOMA: EIGHT YEAR EXPERIENCE

Pedro J. Rosselló, MD, Pedro J. Santiago Borrero, MD and Víctor A. Marcial, MD

Malignancy is the second cause of death in the pediatric age group. Only the leukemia - lymphoma group, and the central nervous system malignancies, are a more common cause of mortality than the solid retroperitoneal tumors: neuroblastoma and nephroblastoma (1). The purpose of this study and communication is to review the experience with neuroblastoma as registered at the Tumor Registry, University District Hospital.

## Methods

All cases with the diagnosis of neuroblastoma were extracted from the Tumor Registry, University District Hospital, for the eight year period of 1968-1975. The clinical records were then retrieved in 18 of 19 cases, and these were analyzed for various factors. During the same period, all cases of malignancies up to age 18 were identified.

## Results

Multiple factors were analyzed and the relationship to survival explored. There were a total of 19 cases identified, an average of approximately 2.4 cases per year. This accounts for 4.2 percent of all malignancies reported in the 0-18 year age group, and made up the 4th

most common group, after leukemia - Hodgkins Disease (56 percent), central nervous system (17 percent), Wilms' tumor (4.7 percent). The average age at diagnosis was 28.7 months, the mean age 30 month, with a range of 1 to 93 months. There was a male preponderance 14 to 5. No clustering as to time or location of occurrence was noted. The primary site of the tumor was identified in 17 cases and distributed as follows: right adrenal 6, left adrenal 2, right retroperitoneum 3, left retroperitoneum 1, pelvis 3, thorax, 2. Abdominal neuroblastoma therefore accounts for 88 percent of the series.

The clinical presentation varied but a predominant sign was abdominal distention or mass, found in 80 percent. The other associated presenting signs and symptoms, include: anorexia (33 percent), abdominal pain (20 percent), vomiting (20 percent), constipation (20 percent), fevers (20 percent), respiratory difficulties (15 percent), weight loss (15 percent). The interval of identifiable symptoms to diagnosis was less than 1 month in 75 percent, one to three months in 18 percent, greater than three months in 6 percent. The diagnostic work up included tests usually performed in more than 75 percent of the cases (I. V. P., skeletal survey and chest film, bone marrow examination) and others less frequently carried out (arteriogram, inferior vena cavagram, barium enemas, VMA determinations, liver scans). Seventeen of nineteen cases could be staged from the information in the records. The staging was done according to Evan's proposal (4). The staging

---

*From the Departments of Surgery, Pediatrics and Radiological Sciences, University of Puerto Rico School of Medicine.*

TABLE I  
RELATION OF STAGE TO SURVIVAL

Stage	No.(percent)	ALIVE			DEAD	
		With Disease	Without Disease	Months from Dx	No.(percent)	Months from Dx
I	1 (6)	-----	1	-/60	-----	-----
II	1 (6)	-----	1	-/15	-----	-----
III	5 (29)	1 (20 percent)	4 (80 percent)	4/32	-----	-----
IV	8 (47)	2 (25 percent)	-----	8/-	6 (75 percent)	11
IVS	2 (12)	-----	1	-/46	1 (50 percent)	5

TABLE II  
RELATION OF AGE TO SURVIVAL

Age (yrs.)	Alive without Disease	Alive with Disease	Dead	Mortality (Min-Max)
0-1	1	2	1	25-75 percent
1-2	2	---	1	33 percent
2 +	4	1	5	50-60 percent

distribution was as follows: Stage I- 6 percent, stage II - 6 percent, stage III - 29 percent, stage IV - 47 percent, stage IVS - 12 percent. Table I shows the relation of stage to survival. The two cases in stages I, II are long term survivors and cures. There are no deaths in stage III, 4 of 5 showing no evidence of disease with a mean follow up at 32 months. One case is alive with disease after only 4 months follow up. Stage IV patients have a 75 percent mortality with an average of 11 months survival for the dead group. Two of eight patients are still alive but with disease after a short follow up of approximately 8 months. There are only

two cases in stage IVS, one alive and cured, the other dead. The overall series survival is 59 percent with follow up of 3-64 months. If one counts all those alive but with evidence of disease as dead, a 41 percent survival emerges. Table II shows the relation of age to survival. If one takes into account only the dead patients, there is a progressive increase in mortality as one looks at the older children. However, if one calculates the other extreme of the curve by considering those alive with disease as eventual deaths, the relation is not as clear. Table III shows the relation of primary site to survival. Abdominal tumors show a higher



TABLE III  
RELATION OF LOCATION TO SURVIVAL

	No.	Alive without disease	Alive with disease	Dead	Mortality
<i>Cervico thoracic</i>	2	2	---	---	0
<i>Pelvis</i>	3	2	1	---	0-33 percent
<i>Abdominal</i>	12	3	2	7	58-75 percent

TABLE IV  
TREATMENT IN RELATION TO STAGE

Stage	Total	Surgery Only	Surgery Chemotherapy	Surgery Chemotherapy Radiotherapy	Biopsy Chemotherapy	Biopsy Chemotherapy Radiotherapy
<i>I</i>	1	1	----	---	----	---
<i>II</i>	1	---	----	1	----	---
<i>III</i>	5	1 *	----	3	----	1
<i>IV</i>	8	1	1	1	2	3
<i>IVS</i>	2	----	1	----	1	---

mortality. The histology of all these lesions, save for one case, was neuroblastoma or ganglioneuroblastoma. The exception was a mature ganglioneuroma. Table IV summarizes the various therapeutic modalities employed in these children in relation to stage of the disease. Stage III cases were treated by a combination of surgery, chemotherapy and radiation except for one dying shortly after surgery. Stage IV patients were treated mainly with chemotherapy, some receiving adjuvant radiation, but with surgery mostly limited to biopsy. Surgery and chemotherapy were mostly used in Stage IVS. Table V summarizes the types of therapeutic modalities em-

ployed. Total or partial excision was possible in one half of the cases. Cytosan and vincristine were the main stay of the chemotherapy effort, with occasional addition of a third agent (adriamycin, actinomycin or methotrexate). Radiotherapy was used to maximal doses of 3000 R.

#### Discussion

Neuroblastoma is an important and interesting tumor of childhood. In most series it accounts for approximately 6-8 percent of pediatric malignancies (1). In our case review,

TABLE V  
TYPES OF THERAPY GIVEN

	No.
A. <i>Surgery</i>	17
<i>total excision</i>	2
<i>partial excision</i>	7
<i>biopsy only</i>	8
B. <i>Chemotherapy</i>	14
<i>Cytosan only</i>	1
<i>Cytosan, Vincristine</i>	8
<i>Cytosan, Vincristine</i> <i>3rd Agent</i>	5
C. <i>Radiotherapy</i>	9

the percentage is smaller (4.2 percent) but this may be due to the age limit used for other malignancies which was taken as 18 years. Neuroblastoma is a peculiar tumor, in that rare (< 2 percent), but well documented spontaneous regressions occur (1, 2). This correlates with a relatively high incidence of occult neuroblastomas found in neonatal deaths from other causes. One of our cases demonstrates this situation: a well localized 2 cm. stage I adrenal neuroblastoma incidentally found at autopsy, in a 28 day old infant who died of congenital heart disease.

The age of presentation in these cases was comparable to those of other series (1, 3, 5, 6, 7). The distribution of primary site was also roughly similar, with 50-90 percent reported as originating intraabdominally (1, 6). In large series the clinical presentation is fairly uniform, an abdominal mass or distention being the major sign encountered. As in our review, there is a decreasing incidence of other signs and symptoms: anorexia, abdominal pain, vomiting, constipation.

The diagnostic workup is extremely im-

portant in the staging of this disease. Evans et al proposed a system, widely used at present (4). Certain parameters are essential for an accurate staging: chest film, skeletal survey, intravenous pyelogram, bone marrow examination, tissue confirmation and accurate description of the extent of the primary disease at exploration. These were documented in a high percentage of the reviewed cases allowing retrospective staging of 18 of 19 cases. Other parameters are not essential for all cases but may give additional information which may be very useful in specific cases: Inferior venocavagram, catecholamine determinations, arteriograms, liver scans. There are several factors that directly affect prognosis: stage, age at diagnosis, site of primary and histology of the tumor (4, 5, 6, 7). Stage at diagnosis is a very important factor, survival directly related to this as follows: (2, 4, 5, 6) stage I, 80-86 percent, stage II, 60-63 percent, stage III, 30-37 percent, stage IV, 5-7 percent, stage IVS, 75-85 percent. Our reviewed cases, although a small series, compares well with these figures. This is similarly the case when one compares survival with age. Large series demonstrate the clear relationship of this factor to survival (2, 4, 5, 6): less than 1 year — 50-75 percent, 1-2 years — 25-30 percent greater than 2 years — 10 percent.

The site is identified as an influencing factor in terms of prognosis in most series (2, 3, 6, 7). However this may be an effect that depends strongly on the stage of disease at the various sites, more advanced stages being encountered in the intraabnormal group than in the others (3, 7). Our reviewed cases appear to show this relation of site to survival, with the highest mortality for the abdominal variety.

The histology of the lesion is a fourth factor that is related to survival, the less differentiated and primitive forms having a higher mortality than the more mature ones (6, 7).

The small number of cases reviewed here do not allow us to draw any conclusions regarding the efficacy of the various therapeutic modalities. With regards to the surgical approaches used there appears to be a suggestion that partial excision might be beneficial in cases where a total cancer resection is not possible. The beneficial effect of this "debulking surgery" might be to give the other modalities a better chance to control a reduced tumor mass. This appears to be more beneficial for this particular tumor than for other cancers (3, 6). Further refinement of therapeutic programs will have to await results from large cooperative studies.

### Acknowledgment

The author would like to acknowledge the help of the staff of the Tumor Registry and the Record Department of the University Hospital.

### References

1. Snyder, W. H., Hastnup, T. N., Pollock, W. F.: Retroperitoneal Tumors in Pediatric Surgery, Mustard et al Editors. Yearbook Medical Publishers. Second Edition.
2. Siuks, L. F.: Neuroblastoma, in Cancer Medicine Holland, Frei (Editors), Lea and Febiger, 1973.
3. Koop, C. E., Schnauffer, L.: Management of Abdominal Neuroblastoma Cancer 35, 905, 1975.
4. Evans, A. E., D'Angio, G. J., Randolph, J.: A Proposed Staging for Children with Neuroblastoma Cancer, 27: 374, 1971.
5. Breslow, N., McCann, B.: Statistical Estimation of Prognosis for Children with Neuroblastoma, Can. Res. 31, 2098, 1971.
6. Wilson, K., Draper, G. J. Neuroblastoma, its natural history and prognosis: A study of 487 cases. Br. Med. Journ. 3: 301, 1974.
7. Swank, R. L., Fetterman, G. H., Sieber, W. K., Kiesewetter, W. B.: Prognostic factors in Neuroblastoma. Ann Surg. 174, 428, 1971.



# CHANGING PATTERNS IN POISONING IN PUERTO RICO 1972-1976

Sidney Kaye, MSc., PhD.

## Summary:

1. In 1976 there were 54 fatal poisonings studied at the Institute of Legal Medicine.
2. 29 suicides (20M:9F) to 17 accidents (13M:4F) and 8 cases in which the manner could not be determined with certainty.
3. Again as in previous years, suicides outnumbered accidents about 2 to 1.
4. Again the male outnumbered females 2 to 1.
5. There were no suicides under 16 years of age and none over 67 years of age.
6. There were a surprising number of persons over 60 yrs. committing suicide. The females preferred parathion and the males preferred barbiturates. This is clearly the reverse of previous years reporting.
7. Most suicides occurred during the years 21-30; 10 (7M and 3F).
8. There were 6 accidental overdose of alcohol deaths; only one youth; and the females are now coming into the picture.  
(4M): 27; 41; 59; 65 yrs.  
(2F): 42; 63 yrs.
9. Only 1 death was due to salicylates; accidental; F(12 yrs.).
10. Most accidents with overdose also occurred during the years 21-30; 8 (7M:1F).
11. There were no accidental poisonings below the age of 12 and this is in contrast to the United States where there are still many accidental fatal poisonings between the ages of 1-6.

We have been keeping records since 1966 of those fatal poisonings that have been determined at the Institute of Legal Medicine (1, 2) and now find that Fatal Poisonings during the last 4 years (1972 through 1976) appear to be on the decrease in Puerto Rico. See Table I. It is considered of great interest (and importance) for us to review these cases from year to year and to recognize and analyze the persistent or changing patterns as to the cause (which poison was involved) and the manner of death (whether accident or suicide) and also the incidence of age and sex of the decedent.

The cause and manner of death seems to vary (somewhat) with the "trend of our times". Large numbers of new drugs and insecticides are now easily available (3); and the increased use of Heroin (morphine derivatives) (4) among our youths in their rebellious attitude toward our established standards had also brought an increase in deaths due to overdose of these drugs. See Table I.

The cause and manner of death also seems to vary with geographic area, either because of availability and use, and/or the habits and customs of specific region. In the United States, it is known that aspirin among children was a very frequent cause of poisoning and resulted in large numbers of death. Recent innovation of "lid proof" bottles greatly reduced these poisonings — but is still a formidable poisoning. Here in Puerto Rico for some reason, we rarely see a death due to aspirin in a *child* (5). We had 1 case of salicylates in 1976 with a young girl of age 12 which was ruled a *possible* accident?

In Puerto Rico thirty years ago, yellow phosphorus ("Pasta Eléctrica") (6), and stry-

TABLE I  
FATAL POISONINGS DETERMINED AT THE INSTITUTE OF LEGAL MEDICINE

Poison	1966	1967	1968	1969	1970	1971	1972	1973	1974	1975	1976
Parathion (deriv)	30	19	28	43	37	33	20	17	2	5	5
Morphine (deriv)	7	15	18	29	33	33	8	2	4	17	14
Ethanol (alcohol)	8	7	7	11	23	11	30	9	6	11	6
Barbiturates (deriv)	3	3	12	12	9	15	10	5	4	1	5
Phenothiazines	0	1	6	3	7	3	6	5	9	8	5
Tricyclic antidepressants	0	1	0	0	0	2	0	2	2	4	1
Carbon monoxide	3	1	2	5	3	1	10	2	3	5	1
Strychnine	4	3	2	5	2	0	1	1	0	3	2
Phosphorus (Y)	5	2	1	1	2	0	2	1	0	1	4
Librium or Valium *	1	1	1	1	0	7	2	2	2	2	1
Doriden	0	3	1	4	4	1	1	0	0	0	0
Arsenic	1	1	0	0	1	1	2	0	0	0	0
Methanol	1	1	0	10	1	0	0	0	0	0	0
Salicylates	0	0	0	1	0	0	0	0	1	0	1
Serax	0	0	0	0	0	0	2	0	0	0	0
Various	6	2	5	5	5	2	10	21	20	9	9 **
Total Poisons	69	60	83	130	127	109	104	67	52	66	54
Total Deaths in P. R.	17,509	16,585	15,721	16,850	18,080	18,050	18,200	19,257	19,490	19,073	19,893
Pop. (Mill.)	2.6	2.6	2.6	2.7	2.7	2.8	2.8	2.8	2.9	3.2	3.2
Autop. I. L. M.	2,106	1,847	1,932	1,991	2,070	2,759	2,916	3,213	3,477	3,501	3,768

\* - With alcohol or other depressant drugs (1 valium & flornal in 1976)

\*\* - Various (Gasoline (1); herbicide (3); Darvon (1); Diazinon (1); pine oil (1); indeterminate poisons (2))

TABLE II  
DISTRIBUTION OF POISONING  
P. R. 1976

*I. SUICIDES: 29 (20M:9F)*

*Parathion: 5 (1M:4F)*

*M: 25 yrs; F: 63; 56; 64; 67      Female 63 yrs: 0.17 percent alcohol*

*Strychnine: 2 (M) (41; 39)*

*Barbiturates: 5 (3M:2F)*

*M: 31; 29; 66      F: 24, 45*

*Phenothiazines: 5 (4M:1F)*

*M: 56, 18, 28, 30      F: 39*

*Phosphorus (Y): 4 (M)(67, 48, 53, 60)*

*Tricyclic antidepressants: 1 (M)(22)*

*Valium & Fiorinal: 1 (F)(24)*

*Darvon: 1 (M)(50)*

*Herbicide: 3 (M)(29, 66, 45)*

*Indeterminate poisons: 1 (M)(58)      Diazinon: 1 (F)(30)*

*II. ACCIDENTAL: 17 (13M:4F)*

*Morphine: 9 (8M:1F)*

*M: 20, 22, 23, 24, 28, 29, 30, 35      F: 26*

*With alcohol: 2 (M)(0.09 percent; 0.16 percent)*

*Ethanol (Alcohol): 6 (4M:2F)*

*M: 27, 41, 59, 65      F: 63, 42*

*Alcohol Percent: 0.20 percent; 0.24 percent; 0.26 percent; 0.28 percent; 0.36 percent*

*Salicylates: 1 (F)(12)*

*Carbon Monoxide: 1 (M)(40)(0.19 percent)*

*III. INDETERMINATE: 8 (M)*

*Morphine: 5 (M)*

*M: 23, 24, 32, 30, 32*

*One with 0.06 percent alcohol*

*Gasolene: 1 (M)(52)*

*Pine Oil: 1 (M)(39)*

*Indeterminate poisons: 1 (M)(33)*

chnine were common poisonings; and today Phosphorus and Strychnine are still used in Puerto Rico even though they both present such a horrible way to die. See Table I.

Parathion (a very potent organic phosphate ester insecticide) (7) had been the number killer in Puerto Rico up until 1973, See Table I. It had then been possible to pur-



TABLE III  
AGE GROUP AND MANNER OF DEATH  
1976

TOTAL Age Groups	MANNER OF DEATH		
	Suicide	Accidental	Indeterminate
0-5 ..... 0	0	0	0
6-10 ..... 0	0	0	0
11-15 ..... 1 (F)	0	1 (F)	0
16-20 ..... 2	1	1	0
21-30 ..... 20 (4F)	9 (3F)	8 (1F)	3
31-40 ..... 9 (1F)	3 (1F)	2	4
41-50 ..... 7 (2F)	5 (1F)	2 (1F)	0
51-60 ..... 7 (1F)	5 (1F)	1	1
61-70 ..... 8 (4F)	6 (3F)	2 (1F)	0
TOTALS 54 (41M:13F)	29 (20M:9F)	17 (13M:4F)	8 (M)

TOTAL CASES: 54 (41M:13F)

Suicide: 29 (20M:9F)

Accidental: 17 (13M:4F)

Indeterminate: 8 (M)

chase this powerful killer (35 mg is the approximate minimum lethal dose for a 150 pound person) (7) at local drugstore, supermarkets or grocery stores, or even at the hardware store. It is an excellent insect killer (but too potent); Malathion or other *much less toxic* insecticides would also kill insects effectively, and they would be much less dangerous to humans. Our local authorities were then finally convinced to prohibit the sale of Parathion "across the counter". Table I shows Parathion to be still a very dangerous poison even though its mortality dropped from 43 in 1969 to 5 in 1976. This is a great decrease and this is very gratifying.

The heroin "abuse and overdose" deaths during 1969-1971 (2, 4) seemed then destined to overtake the first place of Parathion — but somehow this did not happen when Turkey greatly curtailed the cultivation of the "pop-

py"; with a diminished supply, this greatly reduced the number of deaths due to overdose. When Turkey again returned to growing the "poppy seed", our death rate (overdose to heroin) appears again to be on the increase? Morphine in 1976 is now the number 1 cause of death in Puerto Rico by poisoning, See Table I.

Alcohol in the United States has been for many years (8, 9, 10) the number 1 cause of accidental death due to "overdose". This apparently is not so in Puerto Rico — except in 1972 when it peaked to first place. Alcohol is however, the major contributing factor to more than 50 percent of our traffic fatalities (11, 12).

A review for the calendar year 1976 reveals that poisoning was the cause of death in 54 of the cases reported to the Institute of Legal Medicine. This is a much lower mortality

rate than during previous years especially 1969-1972. Table I shows that morphine (heroin) is in first place with 14 deaths even though it had dropped from a high of 33 in 1970 and 1971.

### I. Suicide

Table II shows *suicides* again outnumber accident almost 2 to 1 (29:17); and males again outnumber females 2 to 1 (20:9).

Barbiturates in previous years (1, 2, 13) was the agent of choice for females and parathion (1, 2, 7) was the agent used by males for suicide. This is clearly reversed in 1976.

Even though the sale of parathion had been recently restricted, it is still available and it is strange that it was the agent of choice for 4 elderly women.

Parathion: 5 (1M:4F)  
M: 25 yrs.  
F: 56; 64; 63; 67 yrs.

Barbiturates: 5 (3M:2F)  
M: 31; 29; 66 yrs.  
F: 24; 45 yrs.

Barbiturates was now the preference of males this is in contrast to 1968 when F:M::3:2 and again in 1972 F:M::5:4.

Preference for a milder form of poisoning (perhaps in ignorance) was not so, when there were 4 deaths with Phosphorus (yellow); all males chose this horrible form of death.

4 (M): 67; 48; 53; 60 yrs.

This is again true with strychnine which also presents a horrible death.

2 (M): 41; 39 yrs.

### II. Accident

In the group of accidental poisoning, overdose with morphine was most frequent with 9 (8M:1F). There was not a single teenager, but none the less there still ranged in the young age group.

F: 26 yrs

M: 20; 22; 23; 24; 28; 29; 30; 35 yrs.

There were also 5 cases of morphine death where the manner of death was uncertain.  
5M:23; 24; 30; 32; 32 yrs.

### Acknowledgment

Thanks and acknowledgments are due to Dr. Rafael Criado and Dr. Marino Sorvill, Forensic Pathologists at the Institute of Legal Medicine for their wholehearted cooperation; and to Carmen Castro Santiago, José R. Rodríguez, Lucy Droz, Flor Mattos, and Sylvia Martínez.

### References

1. Kaye, Sidney: Patterns of Poisoning in Puerto Rico (1968). Bol. Asoc. Med. de P. R., 62: 18, 1970.
2. Kaye, Sidney: Changing Patterns of Poisoning in P. R. (1972). Bol. Asoc. Med. de P. R., 66: 64, 1974.
3. Kaye, Sidney: (a). Poisoning in Children, Bol. Asoc. de P. R., 68: 47, 1976. (b). General guide to the diagnosis and treatment of Poisoning. Bol. Asoc. de P. R., 62: 283, 1970. (c). Bedside toxicology (chapter) Pediatrics Clinics of North America, Aug. 1970, W. B. Saunders, Phila.
4. Kaye, Sidney: Heroin overdose on the rise again? (Toxicology of Morphine). Bol. Asoc. Med de P. R., 69: 77, 1977.
5. Kaye, Sidney: Toxicology of Aspirin, Bol. Asoc. Med. de P. R., 64: 78, 1972.
6. Kaye, Sidney: Microchemical determination of Yellow Phosphorus, J. Lab.
6. Kaye, Sidney: Microchemical determination of Yellow Phosphorus, J. Lab. & Clin. Med., 28: 225, 1942.
7. Kaye, Sidney: Toxicology of Parathion, Bol. Asoc. Med. de P. R., 59: 362, 1967.
8. Kaye, Sidney & H. B. Haag: Terminal levels of blood alcohol concentrations in 94 fatal human cases of acute alcohol, JAMA, 164: 451, 1957.
9. Kaye, Sidney: Toxicology of alcohol and the problems of drinking. Military Medicine, 141: 602, 1976.
10. Medico-Legal Bulletin (O.C.M.E. of Virginia), Vol. 26, No. 1, 1977.
11. Kaye, Sidney: Bol. Asoc. Méd. de Puerto Rico: (a). Alcohol levels and fatal traffic accidents (1968) *ibid* - 61: 244, 1969. (b). Drunk pedestrian and driver on our highways in P. R. (1970), 63: 170, 1971. (c). Influence of alcohol on traffic deaths in P. R. (1972), 65: 135, 1973. (d). Sudden drop in alcohol and drug related traffic fatalities in P. R. (1974), 67: 369, 1975.
12. Kaye, Sidney: (a). Incidence of alcohol, drugs and carbon monoxide in traffic fatalities in P. R. (1973), Proc. 6th. Int. Conf. on Alcohol, Drugs & Traffic Safety, Toronto, Sept. 8-13, 1974.
13. Kaye, Sidney: Toxicology of barbiturates, Bol. Asoc. Med. de P. R., 60: 214, 1968.
14. Kaye, Sidney: Handbook of Emergency Toxicology, C. C. Thomas, 3rd. Ed., 3rd. Ptng., 1977.

## NEFROLOGIA 1977

*En el corto espacio de unos 20 años hemos sido testigos del crecimiento vertiginoso de varias áreas en la medicina. Nos toca de cerca la nefrología, especialidad que apenas tenía un nombre que la definiera como tal en el no remoto año de 1965. El crecimiento de la nefrología, al igual que en muchas áreas del quehacer humano, es el maravilloso producto del esfuerzo combinado de muchos individuos y de equipos de trabajo, y donde las generaciones que se siguen unas a otras avanzan las fronteras a manera de un relevo del batón del conocimiento.*

*Gracias a esta ferviente actividad se ha podido comprender mejor la fisiopatología del sistema renal el cual afecta y es afectado a su vez por la homeostasis del cuerpo. Es el primer sistema completo del cuerpo que se beneficia de un reemplazo, imperfecto pero adecuado de su función por medios artificiales y, más aún, es el primer órgano del cuerpo con funciones múltiples que puede ser transplantado exitosamente. El amplio espectro de actividades nefrológicas ha aportado una mejor comprensión en áreas tales como la hipertensión, fallo cardíaco congestivo, homeostasis hormonal del agua y electrolitos, balance ácido base y sus relaciones pulmonares. Todas ellas están tan estrechamente relacionadas en el paciente críticamente enfermo, que su dominio es ahora necesario para poder ofrecer a estos pacientes una mejor oportunidad de sobrevivir.*

*La importancia de la nefrología y de su interrelación con otras disciplinas en el campo de la medicina se pone de manifiesto cada vez más. Bástenos hojear cualquier revista médica para percatarnos de ello. Revistas generales tales como el JAMA, Archives of Internal Medicine, American Journal of Medicine, New England Journal of Medicine, The Lancet, etc., tienen siempre varios artículos y a menudo números completos y suplementos de temas nefrológicos de impacto en la medicina interna.*

*Hay varias revistas dedicadas exclusivamente a temas nefrológicos tales como Kidney International, Nephrology, y Clinical Nephrology. Temas de fisiología renal y trabajo básico de investigación renal es también publicado en las revistas de estas áreas subespecializadas. El Instituto Nacional de Artritis, Metabolismo y Enfermedades Digestivas del Servicio de Salud Pública Federal está publicando anualmente un voluminoso listado de la literatura nefrológica mundial titulado "Kidney Disease and Nephrology Index" donde señalan todos aquellos trabajos relacionados con la producción nefrológica publicada en las revistas nacionales e internacionales.*

*En un pasado no muy lejano, el futuro nefrólogo fue el producto de los programas de cardiología en la mayoría de los casos, urología en otros y endocrinología en algunos. Un pequeño grupo surgía de los laboratorios de investigación de fisiología renal. Mas, sin embargo, los programas de entrenamiento en nefrología han cobrado vida propia y están generando nefrólogos mejor y más redondamente entrenados. Se requiere que este entrenamiento sea de 2 años, después de cumplir con 3 años de medicina interna. Hoy día no hay centro académico de productividad reconocida, que no cuente con su sección de nefrología compuesta por nefrólogos, creados por programas de entrenamiento, netamente nefrológicos.*

*La actividad nefrológica de mayor impacto social, el tratamiento del paciente urémico, ha sido*



*la primera enfermedad de tipo catastrófico que se somete a una cubierta y control nacional bajo los planes "Medicare". Es la primera vez que se extienden beneficios de Medicare por enfermedad a menores de 65 años.*

*Ha sido ardua labor organizar y armonizar los múltiples intereses que se necesitan para la prestación de diálisis y transplantes. Llevar estos tratamientos, sofisticados y costosos, al máximo número de pacientes, al menor costo posible con alta calidad científica y humana, fue un reto lanzado a la comunidad nefrológica por la sociedad. Este reto está siendo cumplido por la comunidad nefrológica, la cual en coordinación con las diferentes agencias federales, estatales, locales e instituciones privadas, ha creado un sistema de prestación de servicios renales, que muy bien puede ser el boceto preliminar de un plan de servicios médicos más abarcador.*

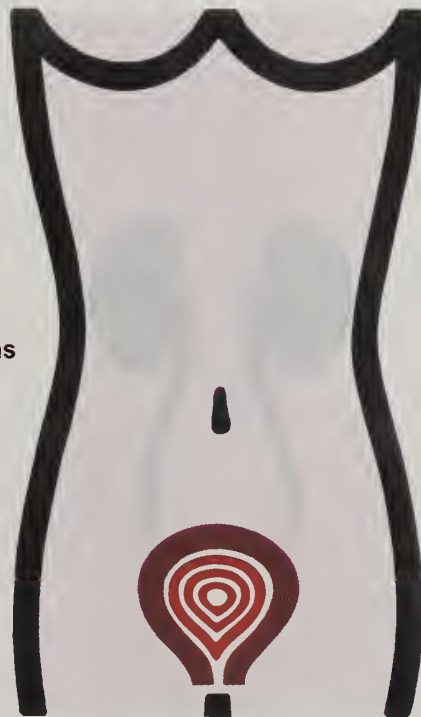
Oswaldo Ramírez Muxó, MD

When pain complicates acute cystitis\*

# Azo Gantanol<sup>®</sup>

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl

for the pain                      for the pathogens



- **Early relief of painful symptoms** such as burning and pain associated with urgency and frequency.

\*Nonobstructed; due to susceptible organisms

- **Effective control of susceptible pathogens** such as *E. coli*, *Klebsiella-Aerobacter*, *Staph. aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*.

- **Appropriate antibacterial therapy:** up to three days therapy with Azo Gantanol, then 11 days with Gantanol<sup>®</sup> (sulfamethoxazole), 0.5 Gm tablets.

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis* and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies.

**Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura,

hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); G.I. reactions (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); CNS reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); miscellaneous reactions (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

**Dosage:** Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**Note:** Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

# TRIAMTERENE CONSERVES POTASSIUM WHILE HYDROCHLOROTHIAZIDE LOWERS BLOOD PRESSURE **DYAZIDE®**

Each capsule contains 50 mg. of Dyrenium® (triamterene, SK&F Co.) and 25 mg. of hydrochlorothiazide.

## MAKES SENSE

Before prescribing, see complete prescribing information in SK&F Co. literature or PDR. A brief summary follows:

### Warning

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

**\* Indications:** When the combination represents the dosage determined by titration: Adjunctive therapy in edema associated with congestive heart failure, hepatic cirrhosis, the nephrotic syndrome. Corticosteroid and estrogen-induced edema, idiopathic edema; hypertension, when the potassium sparing action of triamterene is warranted. (See Box Warning.) Routine use of diuretics in healthy pregnant women is inappropriate; they are indicated in pregnancy only when edema is due to pathological causes.

**Contraindications:** Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

**Warnings:** Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum  $K^+$  levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict  $K^+$  intake. Associated widened QRS complex or arrhythmia requires prompt additional therapy. Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available.

**Precautions:** Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids).

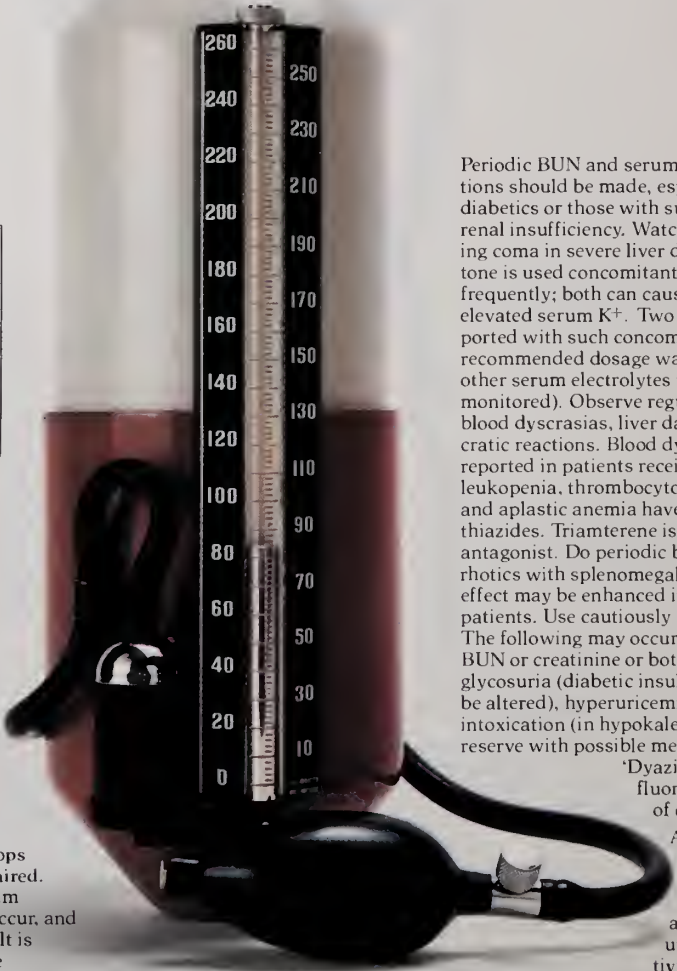
Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Watch for signs of impending coma in severe liver disease. If spironolactone is used concomitantly, determine serum  $K^+$  frequently; both can cause  $K^+$  retention and elevated serum  $K^+$ . Two deaths have been reported with such concomitant therapy (in one, recommended dosage was exceeded, in the other serum electrolytes were not properly monitored). Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic anemia have been reported with thiazides. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effect may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis.

'Dyazide' interferes with fluorescent measurement of quinidine.

### Adverse Reactions:

Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis, rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances. Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and, rarely, allergic pneumonitis have occurred with thiazides alone.

Supplied: Bottles of 100 and 1000 capsules; Single Unit Packages of 100 (intended for institutional use only).



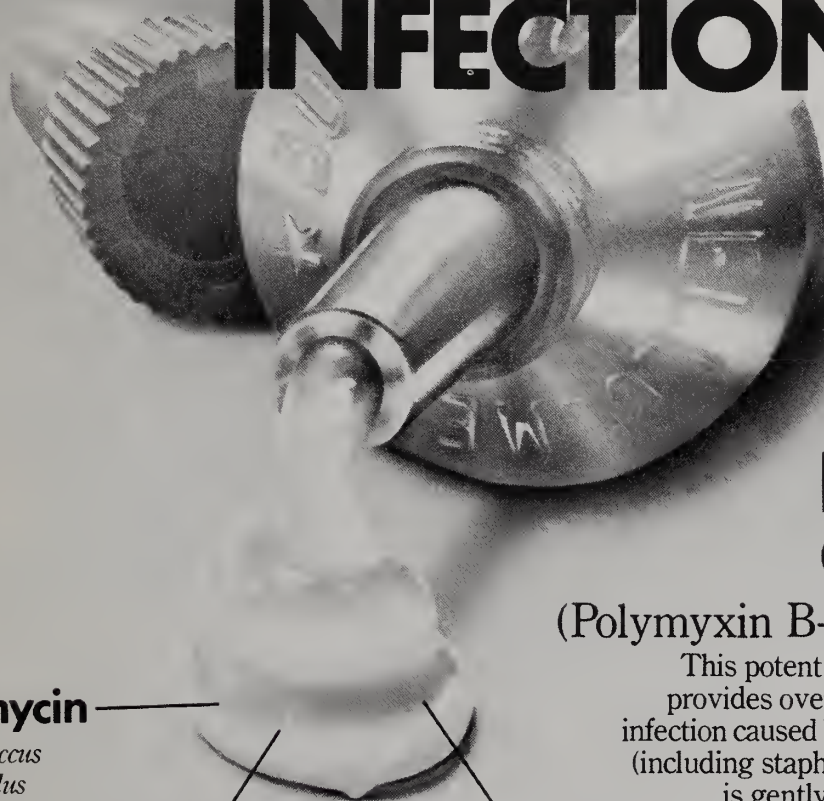
**FOR LONG-TERM CONTROL  
OF HYPERTENSION\*  
SERUM  $K^+$  AND BUN SHOULD  
BE CHECKED PERIODICALLY.  
(SEE WARNINGS SECTION.)**

SK&F CO., Carolina, P.R. 00630

**SK&F CO.**  
a Smithkline company



# THREE-IN-ONE THERAPY AGAINST TOPICAL INFECTION



## Neosporin<sup>®</sup> Ointment

(Polymyxin B-Bacitracin-Neomycin)

This potent broad-spectrum antibacterial provides overlapping action to help combat infection caused by common susceptible pathogens (including staph and strep). The petrolatum base is gently occlusive, protective and enhances spreading.

### Neomycin

*Staphylococcus*  
*Haemophilus*  
*Klebsiella*  
*Aerobacter*  
*Escherichia*  
*Proteus*  
*Corynebacterium*  
*Streptococcus*  
*Pneumococcus*

### Bacitracin

*Staphylococcus*  
*Corynebacterium*  
*Streptococcus*  
*Pneumococcus*

### Polymyxin B

*Pseudomonas*  
*Haemophilus*  
*Klebsiella*  
*Aerobacter*  
*Escherichia*

*In vitro* overlapping antibacterial action of  
Neosporin<sup>®</sup> Ointment (polymyxin B-bacitracin-neomycin).



Wellcome

Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

## Neosporin<sup>®</sup> Ointment

(Polymyxin B-Bacitracin-Neomycin)

Each gram contains: Aerosporin<sup>®</sup> brand Polymyxin B Sulfate 5,000 units; zinc bacitracin 400 units; neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs; in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is

affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



# **OLBY PROCLAIMS WOMAN SUFFRAGE**

**signs Certificate of Ratification  
at His Home Without  
Women Witnesses.**

**MILITANTS VEXED AT PRIVACY.**

**Wanted Movies of Ceremony,  
But Both Factions Are**

**WASHINGTON, Aug. 26, 1920—**  
The struggle for wom-



## **TRUMAN CLOSES UNITED NATIONS CONFERENCE WITH PLEA TO TRANSLATE CHARTER INTO DEEDS**

### **NEW WORLD HOPE**

**President Hails 'Great  
Instrument of Peace,'  
Insists It Be Used**

**HISTORIC LANDMARK**

**Meeting Gives Standing  
Ovation as Executive  
Pictures Peace Gain**

## **Social Security Bill Is Signed; Gives Pensions to Aged, Jobless**

**Roosevelt Approves Message Intended to Benefit 30,000,000  
Persons When States Adopt Cooperating Laws—He Calls  
the Measure 'Cornerstone' of His Economic Program**

### **SENATE APPROVES 18-YEAR OLD VOTE IN ALL ELECTIONS**

**Amendment to Constitution  
is Sent to House, Where  
Passage is Expected**

**WASHINGTON, March 10,  
1971—The Senate approved**

**WASHINGTON, Aug. 14**  
The Social Security Bill, providing a broad program of unemployment insurance and old age pensions and counted upon to benefit 20,000,000 persons, became law today when it was signed by President Roosevelt in the presence of those chiefly responsible for bringing it through Congress.

Mr. Roosevelt called the bill "the cornerstone of my economic program which is being built to give every man's complete right to work."

## **the Draft Ends No**

**WASHINGTON, Jan. 27,  
1973—"With the signing of  
the peace agreement in  
Paris today, and after re-**

"If we fail to use it," he declared to the solemn final meeting of the delegates, "we shall betray all of those who have died in order that we might meet here in freedom and safety to create it."

"If we seek to use it selfishly—for the advantage of any one nation or any small group of nations—we shall be equally guilty of that betrayal."

**Fervent Interpolation**

The President, speaking in the auditorium of the War Memorial Opera House, built in memory of sons of the Golden Gate city who gave their lives in the first World War, in which he himself served, seemed to give unconscious expression to the solemn feeling of the occasion when, at the outset of his speech, he interpolated the words, half a hope, half a prayer:

"Oh, what a great day this can be in history!"

# PATIENT PACKAGE INSERTS: A CONCEPT WHOSE TIME HAS COME?

*The consumer's right to know is an irreversible and desirable trend of the Seventies. It extends, and properly, to a patient's right to know more about his or her prescription medications. One way, gaining favor, is through patient package inserts. Wisely-prepared and properly distributed when medically indicated, they could markedly improve patient knowledge and drug therapy—laudable goals by anyone's standards.*

*The PMA endorses these goals and will work with government, the health professions and consumers to achieve them.*

## **The Advantages**

The concept holds promise of benefits: better patient understanding of the product prescribed, better adherence to the treatment plan, and more awareness of possible side reactions.

Every doctor has had patients who fail to finish antibiotic regimens because they feel better. Some patients assume that if one tranquilizer or analgesic is good, two may be twice as good. Still others fail to report dizziness while on antihypertensive therapy—and so on.

Problems like these might arise less often if the patient received written information in addition to verbal instructions. Some studies suggest that patients are more receptive to such materials, and they more often understand the verbal instructions and follow them, when inserts are used.

## **The Disadvantages**

There are also some potential problems. Obviously, the inserts must be clearly phrased, without extraneous or complex detail. How much information

is enough? How can it be kept current? Should all patients receive the same information? Should inserts be included with all drugs? Should only potential problems be listed or are patients better off with a "fair balance" presentation that describes usefulness as well as drawbacks?

These and similar questions require answers, since model inserts have yet to be properly developed and tested. Despite the need for these studies, the FDA is proceeding prematurely with inserts on selected products. We think the Congress is the only place where the matter can be given the proper legal status and direction, particularly since it represents a conceptual change in the legal, medical and social framework of the nation's prescription drug information system.

## **The Solution**

The PMA believes that carefully-devised pilot studies of various kinds of inserts are needed. They should be developed and implemented with full participation by doctors, pharmacists, consumers, communications experts and the drug industry. Such studies will provide reliable pathways to follow, so that inserts will be useful aids to medical practice.

And particularly we think that you should be closely involved in this debate and in these studies and decisions. Otherwise, people with less experience and qualifications may control the purposes, content and use of a tool with considerable promise for improved patient care. It could make a difference in your practice tomorrow, and more importantly, in the health of your patients.

**PMA**

THE PHARMACEUTICAL MANUFACTURERS ASSOCIATION  
1155 FIFTEENTH ST., N. W., WASHINGTON, D. C. 20005



# DISCURSO DE TOMA DE POSESION COMO PRESIDENTE DE LA ASOCIACION MEDICA DE PUERTO RICO

Rafael Berríos Martínez, MD

Durante el día de hoy finalizan las actividades de nuestra Septuagésima Quinta Convención Anual de la Asociación Médica de Puerto Rico. Sin lugar a dudas este año ha sido un período de intensa actividad y de memorables recuerdos por nuestro Aniversario de Diamante como institución profesional al servicio de la comunidad puertorriqueña. Nuestra brega dentro de la Asociación Médica y en nuestra práctica profesional solo debe tener puntos de partida para redoblar entusiasmo, voluntad y esfuerzo. Invito a todas mis compañeras y compañeros de la Asociación Médica y a todos los que ejercen nuestra profesión a unirse en nuestra institución profesional y a participar activamente en todos sus programas, proyectos y actividades.

Puerto Rico y el mundo entero atraviesan por una época de cambios vertiginosos que nos enfrentan a todos en general, y especialmente a los que practicamos la profesión médica, a nuevos y constantes retos. Los cambios repercuten en todos los aspectos internacionales, regionales, locales y profesionales. Cada día surgen nuevas exigencias en la capacitación profesional del médico, tal y como ocurre en las demás profesiones, aunque quizás en mayor grado en la nuestra. También se desarrollan nuevos enfoques en las relaciones médicos-pacientes, en el desenvolvimiento de las actividades de nuestros dispensarios o consultorios médicos, y en las funciones de los centros hospitalarios. Sin lugar a dudas, los médicos estamos obligados cada vez más a fortalecer nuestra base académica y técnica, a la vez que tenemos que mejorarnos continuamente en nuestras propias cualificaciones psicológicas, mentales y morales.

La trayectoria histórica de la Asociación Médica de Puerto Rico es y debe ser motivo de

orgullo y fuente de inspiración para todos nosotros. Por eso estimo pertinente que evoquemos la memoria de los fundadores de nuestra institución para agradecerles su iniciativa y heroísmo, y a la vez reconozcamos la dedicación y el servicio meritorio de los ex-presidentes que nos acompañan en el mundo de los vivos. Sin embargo, no basta con albergar buenos sentimientos en nuestros corazones porque nuestro deber es trabajar y participar al máximo de nuestras capacidades en el desarrollo y crecimiento de nuestra institución y nuestra profesión. Al recibir el mallete presidencial de mi ilustre predecesor y amigo Emilio A. Arce estoy plenamente consciente de las grandes responsabilidades que conlleva la presidencia de nuestra Asociación Médica de Puerto Rico. Lo más que puedo hacer en este momento es reafirmar mi voluntad de trabajo y sacrificio, recavar la cooperación de todos mis compañeras y compañeros y pedirle a Dios que me conceda fuerzas, energías y capacidad para mantener en alto el prestigio que han forjado mis predecesores para nuestra noble y digna institución.

Las actividades de nuestra Convención Anual han sido vivos ejemplos de lo que podemos hacer en beneficio de la comunidad y de nuestra profesión. Por eso es que el reto del año que se inicia hoy es aún más fuerte porque Puerto Rico entero y la profesión médica en general reclaman y esperan cada vez mayores logros de esta Asociación Médica de Puerto Rico. Lo que se ha logrado y se debe lograr tiene que ser fruto y creación de la labor conjunta de la Cámara de Delegados, la Junta de Directores, las secciones por especialidades, los consejos asesores, y los comités funcionales. La realidad de hoy demanda acción grupal, esfuerzo con-

junto, participación de todos. Solo en esa forma podemos rendirle tributo al pasado, cumplir el deber del presente y proyectarnos al futuro con entusiasmo, optimismo y seguridad.

Si alguna profesión ofrece las mejores oportunidades de integrar pasado, presente y futuro esa es la nuestra y debemos reconocerlo para que este principio nos sirva de guía a cada instante. Solo así podemos rendirle auténtico homenaje a nuestros fundadores, expresidentes y al insigne prototipo de nuestra profesión que es el doctor Ramón M. Suárez, cuyos 60 años de práctica de la medicina celebramos hace apenas 48 horas. Considero que es propio que recordemos aquí algunas ideas del Dr. Suárez, según él las expresara al conmemorarse los 25 años de nuestra Asociación Médica, y las cuales son en síntesis las siguientes: "Nuestra Asociación después de haber entrado no solo a la mayoría de edad, sino a la plenitud de su desarrollo, la ofrecemos al pueblo de Puerto Rico como fuerza poderosa que es, para vigilar por su salud y por su bienestar y la ofrendamos a nuestros hijos como ejemplo de lo que puede la voluntad cuando se pone al servicio del amor a la comunidad y de la ciencia".

Nuestros cimientos, nuestro desarrollo y nuestra proyección al futuro como entidad profesional me llevan a la conclusión de que los servicios de salud no deben clasificarse como una industria, porque la propia naturaleza de nuestra profesión requiere cualidades especiales que van más allá de la elaboración industrial de un servicio. De hecho la profesión médica es en gran medida una combinación inigualable de ciencia y arte, de calidad profesional y de calor humano, de espíritu de sacrificio y de amor al prójimo.

Como seres humanos estamos sujetos a limitaciones y a errores, pero como líderes profesionales de la salud tenemos que superarnos de día a día, y esa es la razón de ser de la Asociación Médica de Puerto Rico a través de sus 75 años de existencia. La meta de nuestra entidad y de cada uno de nosotros ha sido, es y

será la de brindar el mejor servicio médico. Hasta la fecha hemos logrado elevar la calidad de la medicina en Puerto Rico a los niveles más altos posibles y sabemos que la medicina de primera categoría está disponible y debe estar disponible a lo largo y a lo ancho de Puerto Rico, aunque tengamos que resolver en algún momento el futuro, el problema de distribución de servicios médicos en las áreas rurales, ya sea por incentivos especiales para los médicos o por las mejores y más rápidas vías de comunicación y transportación entre las áreas más distantes y los centros urbanos principales. Uno de nuestros principales retos es la necesidad del máximo desarrollo de la medicina preventiva y de la rehabilitación cardíaca, pulmonar, del cáncer y de los problemas mentales. También tenemos que compenetrarnos del uso de todos los mecanismos electrónicos a nuestra disposición colocando las máquinas al servicio de la medicina y cuidándonos mucho de convertirnos en esclavos de las máquinas.

Hoy es preciso que el médico bregue con el paciente como orientador y consejero más que como recetador impersonal y distante. Por aquello de que la historia se repite el médico de hoy tiene que acercarse más al paciente para sembrar la semilla de los valores humanos que pueden y deben ayudar a evitar accidentes, enfermedades del corazón, enfermedades del hígado, crímenes, desórdenes mentales y otras afecciones que son resultado de un estilo de vida deshumanizante y deshumanizado. Tenemos que educar a nuestros pacientes a la vez que nos educamos a nosotros mismos en nuestros hábitos de vida. Tenemos que ayudar a que nuestros semejantes mejoren su calidad de vida para que pueda realmente vivir y no meramente existir. Tenemos que orientar y servir al paciente sin violentar el libre albedrío, porque nuestra función es lograr que cada persona haga voluntariamente lo que debe hacer para proteger su salud.

Para lograr los fines anteriores hay que mantener la educación médica continuada en el más alto nivel de calidad, y por eso estoy con-

vencido de que debemos mantener y fortalecer nuestras comunicaciones con el Departamento de Salud, el Recinto de Ciencias Médicas, las universidades públicas y privadas, el Consejo de Educación Superior, el Tribunal Examinador de Médicos y todas las instituciones públicas y privadas que en una u otra forma tienen que ver algo con la salud del pueblo puertorriqueño. A la vez debemos intensificar nuestra colaboración con todas las profesiones aliadas y unir esfuerzos con los dueños de hospitales, con los administradores de hospitales, con los planes de seguros médicos prepagados y con nuestros pacientes para seguir mejorando la calidad de los servicios médicos-hospitalarios sin que los costos de éstos se eleven a límites incontrolables o irrazonables. Es preciso, además, que concentremos energías para establecer marcos adecuados en la labor de servicio de cuidados intensivos y prolongados, así como en el esfuerzo de prevenir enfermedades y rehabilitar a los pacientes. Debemos estar conscientes de que la calidad no tiene que producir costos exorbitantes, si utilizamos todos los recursos disponibles con la mayor eficiencia. Si logramos establecer un sistema adecuado de servicios públicos y privados para tratamiento ambulatorio o de hospitalización sin excesos en la explotación de recursos y suministros, podríamos controlar los aumentos en costos, a la vez que brindamos un mejor servicio a nuestros pacientes. Creo que hace falta una mejor clasificación y utilización del inventario de recursos existentes en los servicios de salud. Es hora de que nos enfrentemos a la realidad y busquemos soluciones efectivas porque así lo demanda nues-

tra profesión, el gobierno y la comunidad en general.

Los problemas actuales de los servicios de salud requieren cada vez mayor militancia de toda la profesión médica y de la Asociación Médica de Puerto Rico en particular. Por eso exhorto a todos los médicos, tanto en la práctica gubernamental como privada, a que se unan a nuestra Asociación Médica de Puerto Rico y nos ayuden a adoptar las decisiones que demanda nuestro tiempo, por el bien de la salud de nuestro pueblo y por el bien de la profesión médica.

Les invito a pensar en nuevas alternativas para vigorizar nuestra Asociación Médica a través de la verdadera participación. Les pido que me ayuden a continuar la obra que ha llevado a cabo año tras año nuestra institución profesional, y a que la mejoremos, si es posible, no por vanidad individualista o por pequeñeces, sino por misión de grupo y de entidad que tiene la obligación de mantener una continuidad de su obra a la vez que produce nuevas ideas, programas y proyectos para la profesión médica y para la comunidad puertorriqueña. Ayúdenme a estabilizar y acrecentar todo el cúmulo de nuestra gestión diaria con nuestros propios afiliados, con la profesión médica, con el gobierno, con las profesiones afines, con los pacientes y con la comunidad en general. Ayúdenme a incorporar en cada uno de ustedes y en el pueblo de Puerto Rico en general algo más de lo que ya existe en el orgullo y la satisfacción de tener una profesión médica de excelencia y una Asociación Médica que es vanguardia de las instituciones de su clase en el mundo entero.



## N O T A   B I O G R A F I C A



**DR. RAFAEL BERRIOS MARTINEZ**

*Presidente, Asociación Médica de Puerto Rico*

1977

*Nació el doctor Berríos en Yabucoa, Puerto Rico el 28 de febrero de 1931. Realizó sus estudios de Escuela Superior en la Escuela Superior de Yabucoa, donde se graduó en el 1948, pasando a la Universidad de Puerto Rico, donde hizo sus estudios de premédica.*

*Sus estudios profesionales los realizó en la Universidad de Puerto Rico, en la cual obtuvo su doctorado en medicina y cirugía en el año 1956.*

*Su Internado lo realizó en el Hospital de Damas de Ponce, Puerto Rico.*

*Realizó estudios postgraduados de Medicina Física y Rehabilitación en el Hospital de Veteranos de Puerto Rico, Hospital de Veteranos del Bronx, Nueva York; y en el "Georgia Warm Spring Foundation".*

*Prestó servicios en las Fuerzas Armadas de los Estados Unidos de 1957 a 1959.*

*Ha sido distinguido con el premio "Médico del Año" del Comité del Gobernador para el Empleo del Lisiado y el "Libro de Hazañas Doradas" del Club Exchange de Round Hill.*

*Es miembro, entre otras, de la Asociación Médica Americana, de la Sección de Medicina Física y Rehabilitación de la Asociación Médica de Puerto Rico, de la Sociedad de Médicos Graduados de la UPR, de la Sociedad Internacional para la Rehabilitación del Lisiado, de la Asociación Nacional de Rehabilitación de la Asociación de Distrofia Muscular y ha presidido numerosos Consejos y Comités de la AMPR y la Sociedad Médica del Distrito Este.*

## AMA NEWS:

### *MUNCHAUSEN PATIENT BILKS HOSPITALS WITH FANCIED AILMENTS*

CHICAGO — The Munchausen Syndrome has surfaced again, this time in Wilmington, Del. And it was the same man who faked various physical ills to gain hospital admission two years ago in Colorado.

Physicians from the Wilmington Medical Center published an alert to the medical profession in the Sept. 19 Journal of the American Medical Association to be aware that this individual is still at large.

The patient claimed to be a Moroccan oceanographic physicist working with Jacques Cousteau. An intellectual 48-year-old black man speaking with an impressive French accent, he said he was on his way to an oceanographic symposium at Duke University. At the Wilmington Medical Center he complained of pains in the leg and chest and other symptoms, giving a story of having sustained abdominal wounds in the Indochina War necessitating extensive surgery and removal of internal organs. He also claimed a heart attack and heart surgery in Paris.

Doctors in Wilmington became suspicious when the man continued to complain of chest pain and to demand narcotics.

As suspicions were raised, he attempted to call his "personal physician in Casablanca" for advice, and finally left after five days without notifying anyone. A wallet inadvertently left behind contained identification cards from a blood bank in Arizona and a clinic in Massachusetts. Calls to these centers revealed he had also been a patient in them, with similar complaints.

Other cards identified him as "Major F," a "SAC Fighter Pilot and former POW."

On the same day he left the Wilmington Medical Center, he turned up at a local physician's office complaining of narcolepsy and asking pep pills. And the next day he was admitted to the Wilmington Veterans Administration Hospital, where the procedures started over again. He next tried to gain admission to nearby Chester-Crozier Hospital, but officials there already had

been alerted that he was in the neighborhood.

A review of similar cases of patients who fake all sorts of ailments to gain admission to hospitals and doctor's practices revealed that this same individual had been described in a communication in the Journal of the AMA more than two years ago from a hospital in Fort Collins, Colo., where he had gained treatment for his imaginary pains as "Major F, a SAC Pilot and counterintelligence agent." He also had showed up at hospitals in Kansas and Missouri.

The Delaware doctors concluded:

"There is no doubt that this man fits the description for the Munchausen syndrome. Why he seeks a limited supply of amphetamines, what he gains by his dramatic impersonations, and how he obtained so much surgery remain a mystery.

"Although this case was very fascinating to those involved, the continued abuse of medical facilities must not be condoned. We must develop some practical solution for handling these cases which, so far, remain only a medical curiosity."

Reporting on the case are Drs. Herbert H. Heym, Anna W. Sasaki and Dean L. Winslow, of the Wilmington Medical Center.

---

### *WORKER HEALTH TO BE THEME OF AMA FALL CONFERENCE*

CHICAGO — The health of the American worker on his job will be the theme of the 37th Congress on Occupational Health of the American Medical Association Sept. 19-20, 1977, at St. Louis (Stouffer's Riverfront Towers).

The Congress will be cosponsored by the National Institute for Occupational Safety and Health and the Center for Disease Control of the U. S. Department of Health, Education and Welfare.

A highlight of the Congress program will be

the annual awards luncheon, at which the annual award of the President's Committee on Employment of the Handicapped will be presented to Dr. Robert Bennett, Jr., of Atlanta, Georgia.

Program topics will include degenerative diseases and back injuries; work stress and job performance; role of industry in preventing heart disease; toxic compounds in industry; planning for an industrial medical disaster; toxic compounds and the community; and problems of occupational health programs.

Program leaders will include Bruce E. Douglass, MD, of Mayo Clinic; Lee T. Ford, MD, of Barnes Hospital, St. Louis; Herbert C. Modlin, MD, of the Menninger Foundation; James A. Schoenherger, MD, of Presbyterian St. Luke's Medical Center, Chicago; George Roush, Jr., MD, of Monsanto Chemical Co.; Max Klinghofer, MD, of Elmhurst Hospital, Ill.; S. D. Steiner, MD; Clark W. Heath, MD, of the Center for Disease Control, Atlanta; and Carl Zenz, MD, consultant in occupational medicine.

---

#### *OBESE PERSONS LOSE BY FASTING BUT USUALLY REGAIN POUNDS*

CHICAGO — One way to lose a lot of weight in a short time is to quit eating entirely. This will most certainly take off the pounds. The problem is that once the fast ends those pounds invariably creep back on your frame again.

A Los Angeles study project on fasting for gross obesity is reported in the October Archives of Internal Medicine, a scientific journal of the American Medical Association.

Some 207 "morbidly obese" patients — with a mean weight of 330 pounds — went into the hospital for a prolonged fast, up to two months or more without eating. Those fasting for around two months lost a mean of 65 pounds. Those staying with the routine for longer periods lost a mean 99 pounds.

For 12 to 18 months the fasters maintained their reduced weight. And then they began to gain again. Within three years half of the group were back up to their original weight. After seven years only seven patients remained at their reduced weight.

So, if the pounds almost invariably come back,

was the fasting really worth the trouble and expense? It must be done in the hospital and under constant close supervision of a physician. It is definitely not a "do it yourself" program.

Many patients thought the temporary weight loss was worth the effort. It resulted for a time in better health and better quality of life. They were able to find a better job and increase earnings. And those facing necessary surgery were able to survive the operations much better with reduced weight.

Sadly, however, the researchers report that "Normalization of weight with its social and medical benefits and the prolonged abstinence from food failed to alter eating habits or prevent regain." The handful of patients who kept a near-normal weight after the fast required continuous conscious dieting the rest of their lives.

---

#### *SPINAL INJURIES DANGEROUS TO FOOTBALL PLAYERS*

CHICAGO — The young linebacker smashes through the blockers and drives his lowered head into the ball carrier's churning knees to make the tackle.

The crowds cheer the defensive play and the linebacker gets to his feet, apparently unhurt. But he immediately complains of a sharp, burning sensation in his hands and fingers.

Coaches, trainers and team physicians are alerted in the Nov. 7 Journal of the American Medical Association that this burning sensation just might be the only apparent symptom of a spinal cord injury. Not always is there neck pain and paralysis from spinal cord injuries in football, says Joseph C. Maroon, MD, of the University of Pittsburgh School of Medicine.

From 1931 to 1975 there were at least 819 deaths directly related to football participation, says Dr. Maroon. Injury to the brain and spinal cord accounted for almost 80 percent of these deaths. In addition, an unknown number of football players each season are paralyzed for life from spinal injuries, possibly as frequently as one to each 28,000 par-



ticipants, he says.

Dr. Maroon reports on two 17-year-old defensive players who suffered spinal injuries, with the major symptom being a feeling of numbness and burning in the fingers and hands.

Both players recovered, although one required spinal surgery.

"In both of these cases, strength was normal in the legs and reduced only in the arms and hands. If the patient's complaints of burning hands had been disregarded, a partial and incomplete spinal lesion — with potential for complete recovery — may have been converted by improper or injudicious movement, into a complete spinal cord transection and quadriplegia," Dr. Maroon points out.

It is imperative that any athlete with complaints of burning hands be treated as if a spinal fracture were present. On the field, the football helmet should not be removed, but rather used for support of the neck. The face mask can be cut away if necessary to get to the face. Transportation by stretcher or a flat board with at least four persons lifting is essential, he declares.

Prevention of spinal cord injuries should be stressed by the team physician, Dr. Maroon indicates. Coaches must be urged to teach proper blocking and tackling, and to eliminate "goring and spearing." Strengthening and development of the head and neck muscles, particularly in long, slender-necked athletes, should be a prerequisite for football participation. Safe equipment must be provided and properly used.

"It is the responsibility of physicians to instruct all those involved with athletics in the earliest symptoms and signs of spinal cord injuries to prevent that 'second accident' which occurs from improper movement of a patient following a cervical cord injury."

---

#### SWIMMER'S KNEE IS NOW HEALTH HAZARD

CHICAGO — Exercise is mostly good for your

health, but not always.

First it was tennis elbow.

Then came jogger's heel.

And now we have swimmer's knee.

Fortunately, swimmer's knee isn't likely to bother the average swimmer who splashes around the pool occasionally. It is a problem largely for the dedicated competitive swimmer who undergoes an extensive training program. It comes from chronic sprain of a ligament or a pulled hamstring muscle from too much hard swimming.

Sometimes the swimmer can correct the problem by a change in the basic swimming leg stroke. Often, says a communication from Dr. Bernard R. Cahill of Peoria, Ill., in the Nov. 7 Journal of the American Medical Association, there is something mechanically wrong with the swimming stroke that causes the painful knee. In many cases a good coach can cure the problem by an analysis of the stroke, says Dr. Cahill.

---

*THE THIRD MID-WINTER VIRGIN ISLANDS CLINICAL CONFERENCE* will be held in St. Thomas, January 26, 27, 28, 1978 by the U. S. Virgin Islands Medical Society in association with The Faculty of The Johns Hopkins University School of Medicine.

This program is acceptable for 14 credit hours in Category I for the Physician's Recognition Award of the A.M.A., and will include lectures and seminars of interest to the physician in General Practice, Internal Medicine, General Surgery, OB-Gyn and Pediatrics.

For further information, write to: Peter A. Curreri, MD, III Annual Clinical Conference, Box 39, Red Hook, St. Thomas, V. I., 00801.

## AGRADECIMIENTO

*En este año a punto de terminar, la Junta Editora desea expresar su más profundo agradecimiento a todos los patrocinadores del Boletín de la AMPR, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos.*

*La Junta Editora desea expresar igualmente su agradecimiento a los siguientes compañeros médicos que durante el año que termina uos han brindado su desinteresada ayuda y colaboración en la evaluación de los artículos que se nos han sometido. La ayuda brindada por estos compañeros ha permitido una revista de actualidad que refleje la calidad de la medicina puertorriqueña.*

*Para todos, nuestro más profundo agradecimiento.*

Andrés Acosta, M. D.  
Francisco Aguiló, M. D.  
Juan M. Aranda, M. D.  
Robert Axtmayer, M. D.  
Ramón H. Bermúdez, M. D.  
José L. Cangiano, M. D.  
Guillermo Cintrón, M. D.  
Arsenio Comas Urrutia, M. D.  
José L. Corcino, M. D.  
Russel A. Del Toro, M. D.  
Ramón E. Figueroa Lebrón, M. D.  
Herman J. Flax, M. D.  
Rosa Fiol, M. D.  
José M. García Castro, M. D.  
Mario O. García Palmieri, M. D.  
Pedro H. García Pont, M. D.  
B. González Flores, M. D.  
Antonio Grillo, M. D.  
Lillian Haddock, M. D.  
Federico Hernández Morales, M. D.  
George H. Hillyer, Ph. D.  
Luis Isales, M. D.  
Charles D. Johnson, M. D.  
Julio Lergier, M. D.  
Lloyd Le Zotte, Ph. D.

Vornuan I. Maldonado, M. D.  
Manuel Martínez Maldonado, M. D.  
Francisco Olazábal, M. D.  
Luis Oms, M. D.  
Humberto Ortiz, M. D.  
Adolfo Pérez Comas, M. D.  
Guillermo Picó, M. D.  
Elí Ramírez, M. D.  
Osvaldo Ramírez Muxó, M. D.  
José Ramírez Rivera, M. D.  
Carlos H. Ramírez Ronda, M. D.  
Nathan Rifkinson, M. D.  
Angel L. Rivera, M. D.  
Julio V. Rivera, M. D.  
David Rodríguez, M. D.  
Héctor Rodríguez, M. D.  
Angel M. Rodríguez Rosado, M. D.  
Carmen Sáenz de Rodríguez, M. D.  
Juan Rosselló, M. D.  
Eduardo A. Santiago Delpín, M. D.  
José E. Sifontes, M. D.  
José M. Torres Gómez, M. D.  
Jesús M. Vázquez, M. D.  
Rafael Villavicencio, M. D.





A guiló Jr., Francisco .....	311
Alicea, Efraín .....	251
Altieri, Pablo I. ....	129, 258, 276
Aranda, Juan M. ....	281, 308, 327
B angdiwala, Ishver S. ....	10, 319
Befeler, Benjamín .....	281
Bermúdez, Ramón H. ....	70, 87, 134, 222
Berríos Martínez, Rafael. ....	398, 401
Burgos, Francisco .....	4
C ancio, Marta .....	102
Cangiano, José L. ....	29, 241
Cintrón, Guillermo .....	327
Colón, Ana I. ....	113
Colón Rivera, Egidio S. ....	179
Cox, Rafael A. ....	129
D eBakey, M. E. ....	120
Del Toro, Miguel H. ....	145
Defore, W. W. ....	120
E l-Sherif, Nabil. ....	281
F lax, Herman J. ....	96, 152
Font Zelinski, Vicente .....	15
Fortuño, Roberto F. ....	206
Franco, Alejandro .....	379
Fuertes de la Haba, Abelardo. ....	10, 319
G arcía Castro, José M. ....	263, 303
García Rinaldi, R. ....	120, 156
Giraldo, Hernán D. ....	266
Girod, Carlos E. ....	211
González, Migdalia. ....	327
Gorbea, Héctor F. ....	372
Graham, J. M. ....	120

Hernández, Edgardo. . . . .	327
Herrero, Carmelo. . . . .	276
Hiatt, Robert A. . . . .	35
Hillyer, George V. . . . .	74
Howell, Jimmy F. . . . .	156
I turregui Pagán, Juan R. . . . .	206
J avier de Brau, Carmen . . . . .	222
Johnson, Charles D. . . . .	160, 297, 357
K aye, Sidney . . . . .	1, 77, 364, 391
Keillor, Donald W. . . . .	179
L anaro, A. E. . . . .	272
León, José M. . . . .	102
León Rivero, Félix I. . . . .	129
León Valiente, Carlos F. . . . .	55, 70, 87, 134, 237
Linares, Esteban . . . . .	327
Lipes, Jan K. . . . .	35
López Almodóvar, Carlos . . . . .	25
Louis-Gustave, Alain . . . . .	213
Lozada, José A. . . . .	64
M arcial, Víctor A. . . . .	386
Martínez, Ruth . . . . .	113
Martínez Catinchi, Fernando . . . . .	129
Mayol, Pedro . . . . .	251
Menéndez, Rogelio . . . . .	251
Mojica, Víctor M. . . . .	379
Moscoso, Margarita . . . . .	113
Muñiz, Francisco J. . . . .	64
McCollum, C. H. . . . .	120
McIntosh, Henry D. . . . .	167
O rtiz, Armando. . . . .	276
Ortiz Pérez, Héctor . . . . .	319
P inedo, Walter M. . . . .	227
Pérez, Julio E. . . . .	327
Pérez Comas, Adolfo . . . . .	60, 290
Pérez Rodríguez, Felipe . . . . .	222
R amírez Muxó, Osvaldo . . . . .	396
Ramírez Rivera, José . . . . .	145, 188, 191, 199, 266

Ramírez Ronda, Carlos H. . . . .	55, 70, 87, 134, 237, 372, 381
Reyes de Torres, Luz Carlota. . . . .	303
Ritcher, Stanley . . . . .	281
Rivera, Julio V. . . . .	4
Robert, Francisco . . . . .	64
Robles, Rafaela. . . . .	113
Rodríguez, Frank . . . . .	251
Rodríguez Acevedo, Rafael . . . . .	227
Rodríguez Olleros, Angel . . . . .	140
Rosselló, Pedro J. . . . .	83, 233, 386
Roure, Carlos A. . . . .	10, 319
Sánchez Lugo, Fermín . . . . .	303
Santiago, Guillermo . . . . .	10
Santiago Borrero, Pedro J. . . . .	386
Sarmiento, A. H. . . . .	272
Sierra, Radamés . . . . .	379
Sifontes, José E. . . . .	179, 251
Suero, Rómulo . . . . .	276
Taranta, Angelo . . . . .	45
Torres, José M. . . . .	141
Tudo de Lewis, Alma . . . . .	77
Von Koch, L. . . . .	156
Vázquez, D. . . . .	272
Vélez, Wilfredo . . . . .	251
Wright, Kinsman E. . . . .	167



A bstractos: Trabajos a Presentarse en la Asamblea Anual de la AMPR — Nov. 7-12/77, Salón de Convenciones del Condado	331
Acute Pre-Infarction Angina . . . . .	258
Additions for the Elderly, Pitfalls in Prescribing . . . . .	327
Amikacin (BB-K8) and Gentamicin Activity in Vitro Against <i>Proteus</i> <i>Rettingeri</i> , Comparative Study of . . . . .	222
Antibióticos, Diarrea y Colitis Asociada a. . . . .	55
Artificial Insemination Donor . . . . .	227
 B lack Related Diseases, Book Review: Text book of . . . . .	213
Bleeding Duodenal Ulcer in Patient Taking Slow-Releasing Potassium Tablets —, Brief Communication . . . . .	276
 C affeine or Coffee Overdose, Toxicology of . . . . .	1
Cardiac Pacemaker Therapy During Pregnancy Labor and Delivery for Heart Block. . . . .	297
Cat-Cry Syndrome, An Unusual Chromosomal Aberration: Report of a Case and Review of the Literature, The . . . . .	303
Cellular Mediated Immunity in a Normal Adult Population. Evaluation of . . . . .	64
Consentimiento Informado Médico, El . . . . .	15
Contenido . . . . .	408
Coronary Artery Aneurysm: Case Report with Review of Literature . . . . .	129
Coronary Artery Disease: Natural History, Risk Factors and Management . . . . .	167
 D antrolene Sodium: An effective Therapeutic Agent for the Treatment of Spasticity in Children. . . . .	263
Diabetes Mellitus. Revisión y Conceptos Propios, Herencia vs. Ambiente —. . . . .	290
Diarreas Infecciosas Agudas — Diagnóstico y Tratamiento . . . . .	87
Dígalo en Español or "Say It in English" . . . . .	199
Discurso Toma de Posesión como Presidente de la Asociación Médica de Puerto Rico . . . . .	398

<b>E</b>	<b>ditoriales-</b>	
	Dengue . . . . .	381
	Diabetes Mellitus: ¿Herencia o Ambiente? . . . . .	311
	El Consentimiento Informado Médico — Análisis, Defensa y Opinión . . . . .	29
	Esophageal Atresia, Management of Long Segment . . . . .	83
	La Escuela de Medicina ante la Educación Médica Continuada . . . . .	211
	La Hiperlipemia en Puerto Rico . . . . .	141
	Nefrología 1977 . . . . .	396
	Water Contact Patterns and Bilharziasis . . . . .	74
	 Educación Médica del Oeste, Su Historia, El Consorcio de. . . . .	 188
	 Fibrosis Quística en Puerto Rico . . . . .	 251
<b>G</b>	<b>raphics . . . . .</b>	<b>308</b>
<b>H</b>	<b>ealth Maintenance for the Industrial Worker: A Rural Health</b>	
	Experience in Puerto Rico. . . . .	145
	Hematocrit Level for Puerto Rican Women (Age 20-40) . . . . .	319
	Hipertensión, Nuevos Conceptos en la Patofisiología de . . . . .	241
	Hongos Atmosféricos en Puerto Rico — Parte I,	
	Epidemiología de . . . . .	25
	Hyperlipoproteinemic Types Among Puerto Ricans: a Final Report . . . . .	102
<b>I</b>	<b>ndice de Autores . . . . .</b>	<b>415</b>
	Índice de Materias . . . . .	418
<b>M</b>	<b>edical Education: As Developed in The "Curso de Actualización</b>	
	Médica", Evaluation of. . . . .	179
	Medicina en Puerto Rico: 1976, Cómo se Llegó a Ejercer la . . . . .	191
	Morphine), Heroin Overdose on the Rise Again?, Toxicology of. . . . .	77
	Mycotic Pulmonary Artery Aneurysms. A Rare Cause of Fatal	
	Hemoptysis . . . . .	266
<b>N</b>	<b>euroblastoma: Eight Year Experience . . . . .</b>	<b>386</b>
	Nota Biográfica: Dr. Rafael Berríos Martínez . . . . .	401
	Noticias. . . . .	31, 75, 100, 143, 176, 214, 246, 277, 313, 354, 383, 402

O ral and Non-Oral Contraceptives, Intelligence Quotient in Offspring of . . . . .	10
R econocimiento a Arbitros . . . . .	405
Rehabilitación - Filosofía, Alcance y Campo de Acción . . . . .	96
Rheumatic Fever, Recent Advances in the Diagnosis and in the Prevention of . . . . .	45
Right Coronary Artery — Coronary Sinus Fistula with Associated Left Coronary Arteriosclerosis, Successful Repair of a . . . . .	156
Schistosomiasis, Determinants of Human Water Contact Patterns in Urban Puerto Rico with Special Reference to . . . . .	35
Sheehan's Syndrome, Coronary Heart Disease — . . . . .	357
Síndrome de Hipo-neoglucogenia, Carta al Editor: . . . . .	140
Síndrome de Laurence-Moon-Biedl-Bardet. A Propósito de un Caso . . . . .	60
Splenic Injuries in Children, Commentary: Conservative Treatment of . . . . .	233
T emporary Arteritis: Brief Communication . . . . .	379
Tétano: Patofisiología, Clínica, Tratamiento y Prevención. . . . .	372
Thyrotoxicosis with Radioiodine 131, Treatment of . . . . .	4
Trabajadores Incapacitados en Puerto Rico, Programa de las Corporaciones para los . . . . .	152
U retra Posterior, Pólipos de la . . . . .	206
Uso de Drogas entre los Estudiantes de las Escuelas Secundarias de Puerto Rico, Factores Socioepidemiológicos del . . . . .	113
W olff-Parkinson-White Syndrome. Report of Two Cases Treated with Cardiac Pacemakers, Drug Therapy, Cardiac Pacing and Cardiac Surgery in the . . . . .	160





